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CHOLEDOCHOLITHIASIS: MODERN APPROACHES TO DIAGNOSIS, TREATMENT, AND PREVENTION OF COMPLICATIONS AND RECURRENCE: A NARRATIVE REVIEW

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ХОЛЕДОХОЛИТИАЗ: СОВРЕМЕННЫЕ АСПЕКТЫ ДИАГНОСТИКИ, ЛЕЧЕНИЯ, ПРОГНОЗИРОВАНИЯ И ПРОФИЛАКТИКИ ОСЛОЖНЕНИЙ И РЕЦИДИВОВ (ОБЗОР ЛИТЕРАТУРЫ)

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This review synthesizes current evidence to identify unresolved challenges in the diagnosis, treatment, risk prediction, and prevention of complications and recurrence of choledocholithiasis, and to outline priority areas for future research.

Choledocholithiasis occur in approximately 30 % of patients with gallstone disease, with recurrence rates averaging 12.6 %. Magnetic resonance cholangiopancreatography (MRCP) remains the non-invasive diagnostic gold standard; however, its widespread adoption is constrained by high cost and limited accessibility. Machine learning-based risk stratification models represent a promising strategy to optimize patient selection for MRCP and reduce unnecessary procedures.

Among the endoscopic transpapillary treatment methods for choledocholithiasis, endoscopic sphincterotomy plus balloon dilation is the most effective and safe approach. Contact lithotripsy guided by peroral transpapillary cholangioscopy has been shown to have the highest efficacy for stones larger than 15 mm. In surgical management, there is growing interest in single-stage laparoendoscopic rendezvous procedures combining cholecystectomy with endoscopic transpapillary intervention. Although randomized trials have demonstrated their efficacy, broad implementation is hindered by the requirement for hybrid operating suites and the absence of validated patient selection criteria.

Effective prevention of postoperative complications and stone recurrence hinges on the early identification and modifiable risk factors. Existing predictive data remain fragmented, and the development of unified mod-

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els is challenged by complex, non-linear interactions among multiple variables. Machine learning algorithms offer a robust framework to overcome these limitations, with their clinical applicability expanding rapidly due to advances in digital health technologies.

Priority directions for future research in choledocholithiasis management include: personalization of diagnostic and therapeutic algorithms through integration of novel surgical techniques and optimized perioperative care; validation of machine learning-driven predictive models for individualized risk stratification and prevention of complications and recurrence.

Keywords. Choledocholithiasis, endoscopic retrograde cholangiopancreatography, rendezvous technique, biliary stent, machine learning, risk prediction.

Обобщены имеющиеся в литературе данные о ключевых нерешенных проблемах диагностики, лечения, прогнозирования и профилактики осложнений и рецидивов холедохолитиаза.

Среди пациентов с желчнокаменной болезнью холедохолитиаз встречается в среднем в 30 % случаев, частота рецидивов достигает 12,6 %. «Золотым стандартом» диагностики признана магнитно-резонансная холангиопанкреатография (МРХПГ). Однако широкому внедрению метода препятствуют его высокая себестоимость и ограниченная доступность. В этом плане перспективным направлением является применение технологий машинного обучения для стратификации пациентов по группам риска и выбору объективных показаний для МРХПГ.

Среди эндоскопических транспапиллярных методов лечения холедохолитиаза наиболее эффективным и безопасным подходом является эндоскопическая папиллосфинктеротомия в сочетании с баллонной дилатацией. Контактная лазерная литотрипсия под контролем пероральной транспапиллярной холангиоскопии показала наибольшую эффективность при конкрементах размером 15 мм и более. В хирургическом лечении холецистохоледохолитиаза наблюдается интерес к одномоментному подходу – операциям по методике rendez-vous, предполагающим выполнение холецистэктомии и эндоскопических транспапиллярных вмешательств в рамках одной операции. Хотя рандомизированные исследования подтвердили их эффективность, широкое внедрение ограничено необходимостью наличия гибридных операционных и отсутствием четких критериев отбора пациентов.

Для прогнозирования и профилактики послеоперационных осложнений и рецидивов ключевое значение имеет раннее выявление предикторов и их своевременная коррекция. Имеющиеся данные носят фрагментарный характер, а унифицированные модели требуют преодоления ограничений, связанных со сложностью выявления комплексных предикторов и их скрытых нелинейных взаимосвязей. Решением является интеграция методов машинного обучения, применение которых в клинической практике расширяется благодаря прогрессу в области цифровых технологий.

Приоритетными направлениями дальнейших исследований в хирургии холедохолитиаза являются: персонализация диагностических и лечебных алгоритмов, внедрение новых технологий хирургического лечения и оптимизации периоперационного ведения пациентов; валидация прогностических моделей на основе машинного обучения для прогнозирования и профилактики осложнений и рецидивов.

Ключевые слова. Холедохолитиаз, эндоскопическая ретроградная холангиопанкреатография, «рандеву», эндоскопическое билиарное стентирование, машинное обучение, прогнозирование рисков.

INTRODUCTION

The global prevalence of gallstone disease is 6.1 %, which corresponds to a cumulative incidence of 0.47 new cases per 100 person-years of follow-up [1]. Annually, gallstone disease is diagnosed in 6.3 million men and 14.2 million women, with its most common complication, acute calculous cholecystitis, accounting for approximately 200,000 hospi-

talizations [2; 3]. The Russian Federation also demonstrates a persistently high incidence rate, with acute cholecystitis occurring at a frequency of 136 cases per 100,000 adult population [4]. The clinical significance of this issue is underscored by the fact that in 16 % of patients with gallstone disease, cholecystectomy is associated with technical difficulties and a high rate of intraoperative complications [2; 5].

The high prevalence of gallstone disease in the general population also contributes to a substantial incidence of its complications, among which choledocholithiasis (CDL) plays a prominent role, with a reported frequency reaching 30 % [6]. The importance of this pathology is highlighted by its leading position in the etiological structure of acute pancreatitis; the biliary form, associated with CDL, accounts for up to 42 % of all cases worldwide [7]. A separate unresolved issue is the management of patients with obstructive jaundice, with CDL being the etiological cause in 50–60 % of these cases [8; 9]. In patients with acute cholecystitis, the combined incidence of CDL complicated by obstructive jaundice reaches 13.7 % [10].

Key directions in contemporary research include the refinement of diagnostic and treatment algorithms, and the development of personalized approaches for predicting and preventing complications and recurrences based on the identification of individual predictors in patients with CDL. A particularly promising avenue is the integration of artificial intelligence technologies, which could enhance diagnostic accuracy and reduce the number of unnecessary invasive interventions [11–14].

CONTEMPORARY DIAGNOSTIC MODALITIES FOR CHOLEDOCHOLITHIASIS

Preoperative transabdominal ultrasound remains the primary initial diagnostic modality for CDL in the majority of patients [15; 16]. However, its diagnostic value is highly dependent on the skill of the ultrasound specialist, resulting in a substantial rate of false-negative findings in the detection of CDL. Multidetector computed tomography (MDCT) also has a significant limitation, as it cannot reliably visualize radiolucent calculi, thereby reducing its efficacy in this patient population. For intraoperative verification of bile duct stones during cholecystectomy, intraoperative cholangiography is employed, while endoscopic retrograde cholangi-

ography (ERCP) is used during endoscopic transpapillary interventions [17]. Nevertheless, intraoperative cholangiography significantly prolongs operative time (by an average of 22.6 minutes) and is associated with a high frequency of technical difficulties during the procedure [18]. ERCP, in turn, serves as a risk factor for the development of post-ERCP pancreatitis (PEP) [19].

Currently, magnetic resonance cholangiopancreatography (MRCP) is recognized as the non-invasive diagnostic gold standard [20; 21]. Indications for its use include the presence of specific findings on ultrasound or MDCT: common bile duct dilation exceeding 6 mm, obstructive jaundice, elevated transaminase levels on biochemical blood analysis, or a history of acute pancreatitis of biliary etiology [22]. MRCP enables comprehensive assessment of the biliary tract, allowing determination of the level and etiology of ductal obstruction, detailed characterization of individual anatomical variants, evaluation of the severity of inflammatory changes, and differential diagnosis from neoplastic processes [23]. Routine preoperative MRCP in patients with acute calculous cholecystitis significantly increases the detection rate of concomitant CDL (20.7 % vs. 9.9 % with ultrasound) as well as anatomical variations of the bile ducts. This facilitates a reduction in the risk of perioperative specific complications, including intraoperative bile duct injury, PEP, and residual CDL [12]. However, the widespread adoption of MRCP is hindered by its high cost and limited accessibility, which may lead to delays in surgical intervention, prolonged hospital stays, and increased healthcare expenditures [24].

Endoscopic ultrasound (EUS) also demonstrates high diagnostic accuracy in detecting CDL, with a sensitivity reaching 89.5 %, specificity of 96.5 %, and positive and negative predictive values of 91.9 % and 95.3 %, respectively. During surgical intervention, the absence of CDL on EUS can obviate the need for invasive ERCP, thereby reducing the incidence of PEP,

particularly in patients with an intermediate risk of CDL [25]. The primary drawbacks of this modality also remain its high cost and relative technical complexity.

Based on the probability of CDL, patients with gallstone disease are stratified into three risk categories. The high-risk category includes patients presenting with at least one of the following criteria: visualization of a bile duct stone on ultrasound or MDCT, clinical manifestations of cholangitis, or the combination of bile duct dilation and hyperbilirubinemia. ERCP is indicated for this patient group. Intermediate risk is defined by the presence of any of the following: hyperfermentemia (elevated liver enzymes), patient age over 55 years, or bile duct dilation in the absence of hyperbilirubinemia. For patients in this category, additional confirmatory investigations are recommended preoperatively, such as EUS or MRCP, or intraoperative diagnostic modalities including laparoscopic intraoperative cholangiography or intraoperative ultrasound. The low-risk category comprises patients without any of the aforementioned clinical, laboratory, or imaging findings. In these patients, cholecystectomy may be performed without further investigation to exclude CDL. This algorithm optimizes the diagnostic process, avoiding unnecessary invasive procedures in low-risk patients while ensuring timely diagnosis in intermediate- and high-risk groups [26]. It is crucial to note, however, that these criteria were developed for the general population with gallstone disease and may exhibit low specificity in patients with acute calculous cholecystitis [24].

A promising avenue in the diagnosis of CDL and patient risk stratification involves the application of machine learning techniques. Scales developed using random forest algorithms and ensemble models have demonstrated superior performance for this purpose, surpassing the high-risk criteria outlined in the American Society for Gastrointestinal Endoscopy clinical guidelines in terms of accuracy and

specificity. Key predictive variables for high risk of CDL in patients with acute cholecystitis include common bile duct diameter, lipase levels, ultrasound/MDCT evidence of cholelithiasis and CDL, and elevated levels of gamma-glutamyl transferase and alanine aminotransferase [24]. Another machine learning model for CDL diagnosis proposed a simplified version incorporating only three parameters: aspartate aminotransferase equal to or greater than 115 U/L, alkaline phosphatase equal to or greater than 165 U/L, and common bile duct diameter greater than 6 mm [27]. Both models exhibited high discriminatory power. Consequently, the application of machine learning algorithms represents a promising direction for enhancing diagnostic accuracy in CDL and refining patient risk stratification. A significant potential advantage is the ability to reduce the number of unnecessary, costly investigations (such as MRCP and EUS) through more precise patient selection. However, further research involving large patient cohorts is required to confirm the efficacy and facilitate the widespread clinical implementation of these models, as such studies are currently limited in the available literature.

CURRENT SURGICAL TREATMENT STRATEGIES FOR CHOLEDOCHOLITHIASIS

Since the 1980s, ERCP with endoscopic papillary sphincterotomy (EPST) and stone extraction has been the standard treatment modality for patients with CDL [28; 29]. An alternative to EPST is endoscopic papillary balloon dilation (EPBD). This technique allows for stone extraction with less damage to the sphincter of Oddi and, consequently, a lower risk of specific postoperative complications, particularly PEP [30]. However, this method is only indicated as an alternative for bile duct stones smaller than 10 mm [31; 32]. In other cases, a combined technique – endoscopic sphincterotomy plus balloon dilation (ESBD) – is widely used. This approach is superior to isolated EPST in terms

of successful bile duct clearance and, in some instances, eliminates the need for lithotripsy to remove large stones, without a significant increase in the risk of PEP or bleeding from the major duodenal papilla [30; 33]. A randomized controlled trial (RCT) has also demonstrated the efficacy of this method in patients with CDL and juxtapaillary diverticula. Furthermore, the ESD technique results in shorter operative times compared to either EPST or EPBD [34]. The optimal duration of dilation remains a subject of investigation. A recent Bayesian network meta-analysis of RCTs demonstrated that 180 seconds is the optimal duration for both methods, associated with the highest rate of successful bile duct clearance and the lowest risk of PEP [35]. A promising development is the use of innovative devices combining a sphincterotome and a balloon in a single instrument, enabling the combined procedure without instrument exchange, thereby reducing operative time [36].

An important aspect of balloon dilation's efficacy is its impact on the risk of recurrent CDL, which is directly related to the degree of sphincter of Oddi injury. Meta-analytic evidence indicates that EPBD is associated with a lower risk of recurrence compared to isolated EPST, particularly in the subgroup of patients who have undergone cholecystectomy. However, the functional advantage of preserving the sphincter of Oddi is negated when large balloons (equal to or greater than 12 mm) are used [30]. Therefore, ESD is considered a rational compromise.

Isolated EPST or ESD achieves effective and complete bile duct stone clearance in 85–90 % of patients with CDL [37]. However, in 10–15 % of cases, complete stone extraction during the initial endoscopic transpapillary intervention is not feasible due to «difficult» CDL. This term encompasses a wide range of clinical scenarios, including: stones larger than 15 mm in diameter, multiple stones, atypical stone shapes (e.g., barrel-shaped), intrahepatic stone location, Mirizzi syndrome, distal bile duct stricture or

tortuosity (oblique, S-shaped, etc.), the presence of juxtapaillary diverticula, and a history of reconstructive surgical procedures [38–40].

For large and hard stones that cannot be extracted after EPST and/or balloon dilation, stone fragmentation is crucial. Such situations occur in approximately 16.9 % of patients [8]. Mechanical lithotripsy has long been the primary method for fragmenting large bile duct stones. Its overall success rate ranges from 76 % to 91 %, but during initial interventions, success is achieved in only 50–70 % of cases. Additionally, the risk of lithotripsy-specific complications (such as basket impaction or breakage) reaches 3.6 % [38].

Recent advances in intracorporeal lithotripsy techniques, particularly laser and electrohydraulic lithotripsy guided by peroral transpapillary cholangioscopy (PTCS), have significantly improved outcomes for difficult CDL [41–43]. The overall efficacy of contact lithotripsy methods is 90 %. Laser techniques show comparable results: overall fragmentation success with holmium laser is 93.3 %, and with thulium laser, 90 %. Complete bile duct clearance in a single session is achieved in 92.9 % of cases with holmium laser and 88.9 % with thulium laser. Electrohydraulic lithotripsy demonstrates somewhat lower efficacy, with an overall success rate of 86.7 % and a first-procedure success rate of only 61.5 % [44]. Another study reported that PTCS with thulium laser lithotripsy achieved an overall efficacy of 93 % with no observed complications [45]. A comparative study evaluating the SpyGlass system (Boston Scientific, USA) combined with holmium laser versus standard mechanical lithotripsy confirmed the superiority of high-tech contact methods: mechanical lithotripsy was 72 % effective, whereas contact laser lithotripsy was successful in all cases [46].

A recent systematic review and network meta-analysis of treatment outcomes in over two thousand patients with large bile duct stones compared five therapeutic approaches: isolated EPST, EPBD, ESD, mechanical litho-

tripsy, and PTCS-guided contact lithotripsy. The results demonstrated that all modalities except mechanical lithotripsy were more effective than isolated EPST. PTCS-guided contact lithotripsy showed the highest efficacy, particularly for stones larger than 15 mm. ESD ranked second, offering lower costs and greater accessibility in clinical practice. No statistically significant differences were found in the rates of intra- or postoperative complications among the evaluated techniques [47].

According to the European Society of Gastrointestinal Endoscopy clinical guidelines, if complete stone extraction is not possible during the initial endoscopic transpapillary intervention or if the aforementioned methods are unavailable, endoscopic biliary stenting with deferred stone extraction is recommended [29]. This strategy reduces the risk of cholangitis and PEP and may also facilitate stone size reduction through friction against the stent, thereby increasing the success of subsequent interventions. Endoscopic stenting is effective in the majority of such cases. Successful complete bile duct clearance after stenting upon repeat intervention is 79 %, reaching 82 % with the addition of ursodeoxycholic acid therapy [37]. Similar results were obtained in domestic studies analyzing the appropriateness of complete bile duct clearance for «difficult» CDL. An approach involving EPST with stone extraction, and lithotripsy/balloon dilatation, if necessary, demonstrated 86.8 % efficacy with a 4.4 % complication rate. A strategy of primary stenting with deferred stone extraction after 1.5–3 months showed 96.4 % efficacy with a 2.4 % complication risk [48].

However, comparative morphological analysis has revealed that the type of pathological changes in the bile duct wall depends on the stent type. Plastic stents have been shown to induce marked fibrosis and atrophy of all wall layers, as well as significant damage to the ultrastructure of cells regulating ductal motility. Another study demonstrated that repeated and

prolonged stenting for CDL causes progressive structural changes in the liver, ranging from ductal hyperplasia and cholestasis to the formation of portoseptal septa and the development of severe cholangiohepatitis consistent with secondary biliary cirrhosis [49; 50]. Thus, biliary stenting induces irreversible morphological changes both locally (in the duct wall) and systemically (in the liver parenchyma). The nature and severity of these changes depend on the stent material, the duration of stenting, and the number of procedures. This underscores the necessity of limiting stenting duration and carefully selecting the stent type, especially when radical treatment is an option.

STAGING OF SURGICAL INTERVENTIONS FOR CHOLEDOCHOLITHIASIS COMBINED WITH CALCULOUS CHOLECYSTITIS

The current standard of care for patients with calculous cholecystitis and CDL is a two-stage approach, which involves performing endoscopic transpapillary intervention with stone extraction as the first stage, followed by laparoscopic cholecystectomy (LC) as the second stage. Concurrently, there is growing interest within the surgical community in a single-stage approach – procedures using the "rendez-vous" technique – which combines LC and bile duct stone clearance within a single operative session under one anesthetic. This technique has been successfully investigated in large-scale RCTs. However, the results of these studies vary considerably: some reported only a significant reduction in hospital stay, others demonstrated a decrease in the rate of postoperative complications, and still others found reduced treatment costs [51–60]. Based on recent meta-analyses of RCTs conducted on this topic, it can be stated that a sufficiently robust evidence base has now been established, demonstrating the advantages of the single-stage approach compared to traditional two-stage treatment [61–

66]. The most significant benefit is the improved efficacy of complete bile duct stone clearance [66]. Furthermore, meta-analyses unanimously confirm a reduction in the rate of specific postoperative complications with the single-stage approach [62; 64; 65]. Additionally, a notable decrease in the incidence of PEP has been observed [62; 63]. Another significant advantage of the one-step strategy is a marked reduction in the length of hospital stay [63; 64; 66]. This is achieved by performing both interventions under a single anesthetic, eliminating the interval between stages. It is noted, however, that the total operative time for the single-stage approach tends to be longer, attributable to the need for coordination between two surgical teams and the performance of two procedures in one operative session [63]. The clinical guidelines of the Russian Society of Surgeons "Cholecystitis" permit the performance of single-stage operations using the rendez-vous technique.

It is important to note that the concept of single-stage operations for cholecystocholecholelithiasis encompasses two methods: LC combined with laparoscopic bile duct clearance, and LC combined with intraoperative endoscopic transpapillary intervention. However, based on the overall balance of safety and efficacy (rates of complications and successful bile duct clearance), the single-stage approach incorporating LC and intraoperative ERCP is considered optimal [65].

To date, this technique has not gained widespread adoption and its use is largely confined to specialized clinical centers. This is because the successful implementation of a single-stage strategy in broad clinical practice requires the availability of a hybrid operating room and appropriately specialized personnel within the

healthcare facility [67]. Furthermore, widespread implementation is hindered by the challenge of timely preoperative diagnosis of common bile duct stones, related to the limited accessibility of MRCP. Nevertheless, the single-stage approach represents a promising direction, offering the potential to reduce postoperative complications and hospital stays [65; 66]. Future research should focus on optimizing patient selection criteria for each approach and evaluating long-term outcomes, including the rate of recurrent CDL.

PREDICTION AND PREVENTION OF SPECIFIC COMPLICATIONS AFTER ENDOSCOPIC TRANSPAPILLARY INTERVENTIONS

The most frequent and clinically significant specific complication of endoscopic transpapillary interventions is the development of PEP [68; 69]. According to a large meta-analysis of 145 RCTs, summarizing treatment outcomes for 19,000 patients from 1977 to 2022, the overall incidence of PEP is 10.2 %, increasing to 14.1 % in high-risk patient groups. Notably, these figures, as well as the rate of severe forms (0.5 % in the general population) and associated mortality risk (0.2 %), have remained stable for over four decades of observation [70]. Other specific complications of endoscopic transpapillary interventions occur less frequently: bleeding from the major duodenal papilla is observed in approximately 1.5 % of cases, cholangitis in 2.5 %, cholecystitis in 0.8 %, and perforation with biliary peritonitis in 0.5 % [71].

Therefore, despite the variety of potential risks, PEP maintains a leading position both in terms of incidence and impact on clinical outcomes. Risk factors for developing PEP during endoscopic transpapillary interventions include patient age under 50 years, female sex, obesity, absence of bile duct dilation, normal bilirubin levels at the time of the procedure, Haraldsson macroscopic type II, IIIb, or IV of the major duodenal papilla, intradiverticular location of the papillary orifice, bile duct stone diameter great-

¹Ministry of Health of the Russian Federation. Clinical guidelines: Cholecystitis [Internet]. Moscow: Ministry of Health of the Russian Federation; 2024-2025-2026 [cited 2026 Feb 12]. Approved 2024 Nov 22, available at: https://cr.minzdrav.gov.ru/preview-cr/819_1

er than 1.0 cm, the use of intraductal lithotripsy, the use of precut technique following unsuccessful standard ductal cannulation for 5 minutes, unintended pancreatic duct cannulation, and contrast injection into the pancreatic duct [72].

Identifying the optimal strategy for PEP prevention remains a relevant challenge in contemporary surgery. A comparative evaluation of primary prophylactic methods, conducted in a network meta-analysis of 42 RCTs, showed that for intermediate-risk patients, the perioperative administration of a combination of rectal indomethacin and aggressive hydration is most effective. For the high-risk group, the best outcomes were demonstrated by the combination of rectal indomethacin and prophylactic pancreatic duct stenting, as well as diclofenac monotherapy [19]. However, conclusions regarding the efficacy of stenting are inconsistent; another meta-analysis based on individual patient data confirmed a significant protective effect of non-steroidal anti-inflammatory drug therapy and hydration but did not find such an effect for prophylactic pancreatic duct stenting [73]. The prophylactic efficacy of rectal NSAIDs, particularly diclofenac, is also supported by other researchers, who additionally emphasize the importance of a multimodal approach [74].

A key research direction is the development of tools for personalizing the prevention of specific post-ERCP complications. For instance, machine learning methods have been used to create models identifying independent predictors of PEP, such as female sex, arterial hypertension, a history of pancreatitis, and technical difficulties during the procedure [69]. Concurrently, practical scoring systems are being developed that integrate clinical and intraoperative parameters to stratify patients into low, moderate, and high-risk groups [72]. Additional data are emerging from studies analyzing risk factors for various complications. One such study, while confirming known predictors of pancreatitis, identified novel risk factors for

hyperamylasemia, cholangitis, acute cholecystitis, and perforations. Interestingly, in this study, prophylactic pancreatic stenting was associated with increased risk, and traditional factors like younger age and female sex showed no significant association [68]. Another study identified female sex, younger age, the presence of calculous cholecystitis, as well as balloon dilation and nasobiliary drainage, as independent risk factors. Protective factors identified included pancreatic duct stenting and thoracic epidural analgesia [75]. Thus, contemporary research not only compares the efficacy of preventive strategies but also actively develops methods for precise individual risk assessment, which forms the basis for selecting targeted prophylaxis. However, existing data on reliable predictors remain fragmentary, and the creation of unified models requires overcoming limitations associated with the complexity of identifying complex and non-obvious predictors and their hidden non-linear interrelationships.

PREDICTORS OF CHOLEDOCHOLITHIASIS RECURRENCE AFTER SURGICAL TREATMENT

According to a recent meta-analysis, the cumulative incidence of recurrent CDL after endoscopic transpapillary interventions averages 12.6 % [76]. Effective prevention of recurrence is impossible without identifying key predictors and developing measures to eliminate or minimize their impact. Pathophysiologically, the occurrence of recurrent CDL is generally divided into two main mechanisms. The primary mechanism is associated with factors such as sphincter of Oddi dysfunction, duodenobiliary reflux, and migration of intestinal microbiota into the bile ducts. The secondary mechanism is attributable to stone migration from the gallbladder in the presence of concomitant calculous cholecystitis [77]. Migrating intestinal microbiota, particularly enterococci, fusobacteria, and *Neisseria* species identified as significant markers in recurrent CDL, can substantially

modify the biliary environment. These microorganisms, possessing resistance to the bactericidal action of bile acids, can initiate and sustain local inflammation, promote bilirubin deconjugation and precipitation of its salts, and alter cholesterol metabolism. An important aspect is the formation of specific dysbiosis, characterized not only by an increased proportion of opportunistic taxa but also by a reduction or absence of protective representatives such as lactobacilli, disrupting microbial homeostasis. Functional metagenomic analysis indicates concomitant changes in the metabolic pathways of the microbial community, including activation of glycan synthesis and disruption of amino acid metabolism, creating additional lithogenic potential. Thus, duodenobiliary reflux acts not only as a mechanical factor but also as a route for the translocation of a complex of intestinal microorganisms, whose subsequent proliferation and altered functional activity in the context of sphincter of Oddi dysfunction become a key element in the pathogenesis of primary recurrent CDL [78; 79].

Results from various clinical studies demonstrate considerable heterogeneity, both in recurrence rates (ranging from 2.8 % to 20 %) and in the spectrum of identified risk factors. In a long-term prospective study by an Italian author group, the recurrence rate of CDL over 5 years of follow-up was 2.8 %. A common bile duct diameter of 22 mm or greater was identified as the sole significant predictor of recurrence [80]. A larger retrospective analysis from Japan with a median follow-up of 3.9 years reported a recurrence rate of 11.3 %. The authors identified a different set of significant predictors: a history of cholecystectomy or current calculous cholecystitis, performance of mechanical lithotripsy, and the presence of postoperative pneumobilia [81]. In a study from the China, the recurrence rate was 6.9 %. Independent predictors included comorbid conditions (diabetes mellitus, fatty liver disease, cirrhosis), smoking, presence of intrahepatic stones, endo-

biliary stenting, and balloon dilation of the bile duct orifice [82]. However, another study from China demonstrated a high CDL recurrence risk of 15.2 %. Significant predictors identified were: advanced age, common bile duct diameter of 15 mm or greater, presence of two or more stones, juxtapapillary diverticula, prior biliary tract surgery, and strictures of the common bile duct or major duodenal papilla [83]. The importance of age as a factor was also confirmed in a study from Israel, where recurrence developed in 20 % of elderly patients compared to only 4 % in a younger cohort [84]. The variability in findings across different studies is attributable to population characteristics, differences in study design, clinical profiles of included patients, and lengths of follow-up.

The size of the EPST performed deserves particular attention as a risk factor for CDL recurrence. A study employing propensity score matching (PSM) demonstrated a statistically significant difference in recurrence rates: in the group with a small incision, recurrences developed in 17.0 % of cases, compared to 6.4 % in the group with a medium-sized incision. Multivariate analysis confirmed that a medium-sized EPST is an independent protective factor against CDL recurrence [77].

Studies focusing on laparoscopic common bile duct exploration report substantially lower recurrence rates compared to endoscopic techniques. The cumulative incidence of recurrence after this approach is 1.34 %, 4.36 %, and 7.14 % at 1, 3, and 5 years, respectively. Significant predictors of recurrence included age, T-tube drainage, hepatic steatosis, urolithiasis, post-cholecystectomy state, and importantly, prior EPST. This latter factor points to the key role of sphincter of Oddi dysfunction in the pathogenesis of recurrence [85]. A thirty-year prospective study demonstrated an overall recurrence rate after laparoscopic common bile duct exploration of 3.8 %. Independent predictors of recurrence were identified as choledochotomy access, use of a T-tube, and again, prior EPST. The

authors conclude that strategies preserving the functional integrity of the sphincter of Oddi are advantageous [86].

Contemporary international research expands the understanding of CDL recurrence pathogenesis by incorporating the additional role of systemic homeostatic disturbances. A multicenter study using PSM identified a significant association between high recurrence risk and levels of total cholesterol and glycated hemoglobin [87]. Another study, among other factors, identified hypoproteinemia as an independent predictor of recurrence [88]. Furthermore, the influence of concomitant obesity on the risk of CDL recurrence has been demonstrated [89]. Additional risk factors recognized include a sedentary lifestyle, high-fat diet, alcohol consumption, and low vegetable intake in the postoperative period, underscoring the importance of lifestyle modification [90]. Among protective factors, the efficacy of ursodeoxycholic acid therapy [91], as well as statins and aspirin, has been demonstrated, pointing to potential avenues for pharmacological prevention of CDL recurrence [87].

To systematize the accumulated heterogeneous data on predictors of CDL recurrence, a large-scale meta-analysis was conducted by a research group from the China. This resulted in a proposed classification of predictors by level of evidence. Strong risk factors identified included a common bile duct diameter of 15 mm or greater, an acute bile duct angulation, the need for repeat endoscopic transpapillary interventions to achieve complete stone clearance, the presence of postoperative pneumobilia, prior biliary tract surgery, and endobiliary stenting. The category of moderate predictors comprised a dilated (but less than 15 mm) common bile duct diameter, presence of a juxtapapillary diverticulum, mechanical lithotripsy, and performed cholecystectomy [92].

Thus, current evidence indicates a multifactorial nature of CDL recurrence, contributed to by local anatomical and functional changes

in the biliary tract, systemic metabolic disturbances, and technical aspects of the performed endoscopic transpapillary intervention. However, as presented above, existing data on reliable predictors remain fragmentary. In this context, the implementation of machine learning algorithms offers new opportunities for identifying complex, non-linear relationships among multiple variables [93; 94]. Currently, despite active investigation into the application of machine learning for CDL diagnosis and bile composition analysis [24; 95–97], validated models for predicting individual risk of CDL recurrence after surgical treatment are scarce in the available literature. Models based on the random forest algorithm have demonstrated the highest efficacy. Using SHAP (Shapley Additive exPlanations) analysis, three key predictors of recurrence were identified: stone size greater than 15 mm, common bile duct diameter greater than 15 mm, and direct bilirubin level [98]. Therefore, further development of such prognostic tools based on machine learning technologies represents a relevant and promising direction for improving the prevention of CDL recurrence [99]. Future research should focus on integrating disparate risk factors into unified prognostic algorithms, including through the application of machine learning, to personalize preventive measures.

CONCLUSION

The present analysis of contemporary data demonstrates that, despite significant progress in the diagnosis and treatment of CDL, a number of unresolved issues persist, necessitating targeted further research. Key directions include the development and validation of integrated, personalized algorithms to optimize diagnostic workup and treatment strategies based on accurate stratification of individual risks for complications and recurrence. In-depth investigation of the pathogenetic mechanisms of recurrence, including the role of du-

odenobiliary reflux, the biliary microbiome, and systemic metabolic disturbances, appears promising for the creation of targeted preventive strategies. A comprehensive evaluation of the efficacy and safety of new technologies, such as single-stage simultaneous operations, contact lithotripsy under cholangioscopic guidance, and stents with intrinsic antimicro-

bial properties, warrants particular attention. Furthermore, the implementation and clinical validation of prognostic models based on artificial intelligence, capable of identifying complex nonlinear relationships among multiple factors, is a necessary condition for transitioning to personalized medicine and improving long-term outcomes for patients with CDL.

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