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MULTIMODAL MANAGEMENT OF BENIGN OBSTRUCTIVE JAUNDICE: A SYNTHESIS OF CURRENT EVIDENCE

MANAGEMENTUL MULTIMODAL AL ICTERULUI MECANIC BENIGN: SINTEZA DOVEZILOR ACTUALE

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ABSTRACT

Objectives. To synthesise contemporary evidence on triage, risk stratification and combined therapeutic strategies in benign obstructive jaundice, and to formulate a set of practical desiderata adaptable to the resource context of the Republic of Moldova.

Methods. Structured narrative review of the literature published between January 2010 and August 2026, searching PubMed/MEDLINE, Embase and the Cochrane Library. Professional society guidelines, Cochrane systematic reviews, meta-analyses, randomised controlled trials and external guideline validation studies were prioritised. Reference protocols were compared on the points where their recommendations diverge.

Results. The Tokyo Guidelines TG18 remain the most widely validated triage instrument for acute cholangitis, and biliary drainage performed within the first 48 hours is associated with lower in-hospital mortality (OR 0.52; 95% CI: 0.28–0.98). The ASGE and ESGE criteria show modest discriminative power in high-risk patients, their principal strength lying in ruling out choledocholithiasis in low-risk patients. Selective biliary cannulation fails in 5–15% of procedures, an intradiverticular papilla reducing the success rate to 80.1% compared with 88.7% in the absence of a diverticulum. Primary closure of the choledochotomy is associated with fewer retained stones (OR 0.57), less biliary peritonitis (OR 0.22), and shorter operative time and hospital stay. Cholecystectomy performed within 72 hours of endoscopic clearance reduces conversion to open surgery (RR 0.35) and recurrent biliary events (RR 0.09).

Conclusions. Contemporary management of benign obstructive jaundice requires rigorous triage, dynamic stratification of operative risk and sequential integration of therapeutic components. In centres where the necessary infrastructure and expertise are already available, the desiderata with the largest demonstrated effect depend mainly on the organisation of the patient pathway.

Keywords: benign obstructive jaundice, choledocholithiasis, endoscopic retrograde cholangiopancreatography, acute cholangitis, quality of life

REZUMAT

Obiective. Sintetizarea dovezilor contemporane privind triajul, stratificarea riscului și strategiile terapeutice combinate în icterul mecanic benign, cu formularea unui set de deziderate practice adaptabile contextului de resurse din Republica Moldova.

Metode. Revizuire narativă structurată a literaturii publicate între ianuarie 2010 și august 2026, prin interogarea bazelor PubMed/MEDLINE, Embase și Cochrane Library. Au fost prioritizate ghidurile societăților profesionale internaționale, revizuirile sistematice Cochrane, meta-analizele, studiile randomizate controlate și studiile de validare externă a ghidurilor. Protocoalele de referință au fost confruntate pe punctele în care recomandările lor diferă.

Rezultate. Ghidurile Tokyo TG18 rămân instrumentul de triaj cel mai larg validat pentru colangita acută, iar drenajul biliar efectuat în primele 48 de ore se asociază cu o mortalitate intraspitalicească mai redusă (OR 0,52; II 95%: 0,28–0,98). Criteriile ASGE și ESGE au putere discriminativă modestă la pacienții cu risc înalt, forța lor principală constând în excluderea litiazei la pacienții cu risc scăzut. Canularea selectivă a căii biliare eșuează în 5–15% dintre proceduri, papila intradiverticulară reducând rata de succes la 80,1% față de 88,7% în absența diverticulului. Închiderea primară a coledocotomiei se asociază cu mai puțină litiază reziduală (OR 0,57) și peritonită biliară (OR 0,22), cu durată operatorie și spitalizare mai scurte. Colectectomia efectuată în primele 72 de ore după asanarea endoscopică a căii biliare (clearance) reduce conversia la chirurgie deschisă (RR 0,35) și evenimentele biliare recurente (RR 0,09).

Concluzii. Managementul contemporan al icterului mecanic benign impune triaj riguros, stratificare dinamică a riscului operator și integrarea secvențială a componentelor terapeutice. În centrele care dispun deja de infrastructura și expertiza necesare, dezideratele cu cel mai mare efect demonstrat depind în principal de organizarea traseului pacientului.

Cuvinte-cheie: icter mecanic benign, litiază coledociană, colangiopancreatografie retrogradă endoscopică, colangită acută, calitatea vieții

Introduction

Benign obstructive jaundice denotes non-malignant obstruction of extrahepatic bile flow, with cholestasis as its consequence. The complications are severe: biliary sepsis, secondary biliary cirrhosis, hepatorenal syndrome, multiorgan dysfunction. In principle the disease is curable. The risks of an untreated course nonetheless require rigorous stratification of patients and individualised therapeutic planning [1].

The condition now lies at the border between interventional gastroenterology, interventional radiology and hepatobiliary surgery [1, 2]. Combined treatment follows from that position. Endoscopy, laparoscopy and open surgery are used in sequence or together, and the choice among them depends on the biological status of the patient and on operative risk. Locally available expertise weighs as heavily.

Gallstone disease provides the majority of the substrate. A meta-analysis of 115 studies, with more than 32 million participants, places the global prevalence at 6.1% (95% CI: 5.6–6.5%); women are affected more often (7.6% versus 5.4%) [3]. In the United States, population data show that the prevalence of gallstone disease and the rate of cholecystectomy have risen over the last three decades [4]. Among patients operated on for gallbladder stones, between 10% and 18% have concomitant stones in the common bile duct (CBD) [5, 6]. Cholecystectomy itself produces iatrogenic biliary injury: 0.3–0.7% of laparoscopic procedures [7].

The aetiology also includes postoperative biliary strictures, Mirizzi syndrome, chronic pancreatitis of the pancreatic head, primary sclerosing cholangitis and post-transplant anastomotic strictures [8, 9]. In the Eastern European area, hepatic hydatid cyst opening into the biliary tree is added [1]. The Department of Surgery no. 2 of the Nicolae Testemitanu State University of Medicine and Pharmacy identified Mirizzi syndrome in 44 patients (0.27%) from a series of 16,346 calculous cholecystitis cases operated on between 1990 and 2010 [9]. Benign strictures of the extrahepatic bile ducts accounted here for 213 patients treated between 1980 and 2010 [8].

The present review examines contemporary evidence on triage, on risk stratification and on combined therapeutic strategies. From that comparison follows a set of practical desiderata that can be verified in a given department.

Materials and methods

A structured narrative review of the literature was performed. PubMed/MEDLINE, Embase and the Cochrane Library were searched for works published between 1 January 2010 and 31 August 2026; the last search was run

on 5 September 2026. The search strategy combined MeSH descriptors and free terms: ("obstructive jaundice" OR "biliary obstruction" OR "choledocholithiasis") AND ("endoscopic retrograde cholangiopancreatography" OR "ERCP" OR "common bile duct exploration" OR "rendezvous" OR "cholecystectomy") AND ("guideline" OR "meta-analysis" OR "systematic review" OR "randomized controlled trial"). Additional searches were run for the terms "acute cholangitis", "bile duct injury", "periampullary diverticulum", "difficult cannulation" and "quality of life", and the reference lists of the retained works were examined manually.

Guidelines of international professional societies (ASGE, ESGE, SAGES, EAES, WSES, ERAS Society, Tokyo Guidelines, British Society of Gastroenterology), Cochrane systematic reviews, meta-analyses, randomised controlled trials, large population-based cohort studies and external guideline validation studies were included, in English, Romanian and Russian. Isolated case reports, series of fewer than 20 patients, studies devoted exclusively to malignant biliary obstruction and works without available full text were excluded. No guideline specific to the EAES and no Russian-language source met these criteria.

By exception from the search interval, seven works published before 2010 were admitted, retained for their foundational character and for the absence of updated substitutes: three works defining assessment instruments still used today in their original form (Charlson comorbidity index, 1987; Portsmouth-POSSUM score, 1998; Gastrointestinal Quality of Life Index, 1995), two works of clinical and pathophysiological reference (the series on morbidity and mortality in surgery for obstructive jaundice, 1983; the synthesis on intestinal permeability in cholestasis, 2007), the only randomised study identified on the route of administration of vitamin K (2002) and the reference publication of the national surgical school on benign obstructive jaundice (2005).

The records obtained were assembled into a common bibliographic file, and duplicates were removed automatically, by matching DOI and PMID identifiers, and subsequently by hand, by comparing first author, title and year of publication. Selection, by examination of titles and abstracts followed by full-text reading, was performed independently by I.C. and A.F., with disagreements resolved by consensus.

National sources not indexed in the international databases were identified separately in the institutional repository of the Nicolae Testemitanu State University of Medicine and Pharmacy, in the electronic archive of the journal Arta Medica and in the register of national clinical protocols of the Ministry of Health; those reporting original case material or management applicable to the national context were retained.

In keeping with the narrative character of the synthesis, the number of records identified and excluded at each stage was not counted systematically. Sixty-four sources were cited: 16 guidelines or consensus documents, 4 Cochrane systematic reviews, 15 other meta-analyses and systematic reviews, 3 randomised controlled trials, 11 observational or external validation studies, 4 works defining the assessment instruments used, 3 narrative syntheses of pathophysiology and 8 national sources.

The comparison of protocols addressed six decision points established in advance: the timing of biliary drainage in acute cholangitis, stratification of the probability of choledocholithiasis, intraoperative cholangiography, the choice between the single-stage and the two-stage approach, closure of the choledochotomy and the timing of cholecystectomy after endoscopic clearance. For each point, the recommendation, its strength and the declared certainty of the evidence were extracted into a comparative matrix. Pairs of guidelines addressing the same point were compared (for example, ASGE, ESGE and the British guideline for risk stratification; the Tokyo Guidelines and the ASGE cholangitis guideline for the timing of drainage; the multi-society Safe Cholecystectomy guideline and the SAGES guideline for intraoperative cholangiography). Divergence was taken to mean the formulation, for the same point, of recommendations of opposite direction or of different strength, or the abstention of a guideline from formulating a recommendation; each divergence was set against the available external validation studies.

The work does not constitute a systematic review in the sense of the PRISMA statement: no prospective protocol was registered, no selection flow diagram was drawn up, risk of bias was not formally assessed and no quantitative synthesis was performed. This limitation is discussed in the Discussion section.

Results

Pathophysiology of cholestasis and implications for operative risk

The cellular and systemic injury produced by biliary obstruction bears directly on operative prognosis [10]. Hydrophobic bile acids accumulate, chiefly chenodeoxycholic acid and deoxycholic acid; their effect on cell membranes is detergent-like and leads to hepatocyte death through apoptosis and necrosis [10, 11]. The injured hepatocyte synthesises vitamin K-dependent coagulation factors deficiently. To this is added malabsorption of fat-soluble vitamins, which aggravates the coagulopathy and the haemorrhagic risk of major interventions.

Hepatic stellate cells and Kupffer cells are activated, and the pro-inflammatory and profibrotic response they sustain, mediated by TNF- α , IL-6 and TGF- β , progresses in neglected chronic forms towards secondary biliary cirrhosis [10, 11]. Bile salts are absent from the intestinal lumen. The microbiome and mucosal permeability change, and endotoxins pass into

the portal circulation [12]. This is the substrate of acute cholangitis and of the systemic inflammatory response, which may progress to septic shock, disseminated intravascular coagulation and acute kidney injury [13, 14].

A prospective observational study of 40 patients with obstructive jaundice documented a diminished monocyte cytokine response to lipopolysaccharide stimulation, with reduced occludin expression and shorter duodenal villi; after endoscopic biliary drainage, the pro-inflammatory response improved [15].

Circulating bilirubin and endotoxins produce renal vasoconstriction and tubular injury. An aggressive intervention in an unresuscitated, deeply jaundiced patient may therefore precipitate postoperative acute renal failure, a complication with unfavourable prognosis documented as early as the classical series [16]. Coagulopathy, biliary sepsis and hepatorenal syndrome are the mechanisms through which the timing of decompression and the match between method and biological stage act on prognosis.

Triage and risk stratification

Some patients require emergency biliary decompression, others prior biological optimisation. Separating them early is the decision with the greatest effect on morbidity and mortality [17, 18].

The most widely validated instrument for clinical and biological triage remains the Tokyo guideline, in its TG13 and TG18 versions. The move from the TG07 to the TG13 criteria raised diagnostic sensitivity from 82.8% to 91.8% and lowered the rate of false-positive results in patients with acute cholecystitis from 15.5% to 5.9% [19]. Charcot's triad, by comparison, has a sensitivity of only 26.4%, with a specificity of 95.6% [19]. Table 1 presents the TG18 criteria.

Grading has quantifiable prognostic consequences. Nine observational studies with 7,534 patients were analysed together: biliary drainage performed within the first 48 hours is associated with lower in-hospital mortality (OR 0.52; 95% CI: 0.28–0.98) and with a hospital stay shorter by 5.56 days (95% CI: 1.59–9.53). For 30-day mortality and for organ failure, the differences did not reach the threshold of significance [21]. The admission-to-drainage interval can be monitored as a quality indicator. The comparison in that meta-analysis was between emergent and urgent ERCP, and the 48-hour cut-off comes from observational cohorts and not from a randomised design [21]. It should be read as an operational threshold rather than as a biological boundary. TG18 itself grades the urgency instead of fixing a single interval: drainage without delay in grade III, early drainage in grade II, and drainage in grade I only if medical treatment fails within the first 24 hours [17, 20].

The grade III criteria belong to the Tokyo guideline. The quick Sequential Organ Failure Assessment (qSOFA) score has a different role, that of screening for sepsis [13].

In patients without clinically manifest cholangitis, ASGE and ESGE stratify the probability of stones in the CBD. The aim is to avoid purely diagnostic endoscopic retrograde cholangiopancreatography (ERCP), a procedure with an

Table 1. TG18 criteria for the diagnosis and severity grading of acute cholangitis, with implications for the timing of drainage

Component	Content
A. Systemic inflammation	A-1: fever ($>38^{\circ}\text{C}$) and/or rigors; A-2: leucocytosis or leucopenia, raised CRP
B. Cholestasis	B-1: jaundice (total bilirubin $\geq 2\text{ mg/dL}$); B-2: ALP, GGT, AST, ALT $>1.5 \times \text{ULN}$
C. Imaging	C-1: biliary dilatation; C-2: evidence of aetiology (stone, stricture, stent, foreign body)
Suspected diagnosis	One item from A, together with one item from B or C
Definite diagnosis	One item from A, together with one item from B and one from C
Grade III (severe)	Dysfunction of at least one organ or system: cardiovascular (hypotension requiring dopamine $\geq 5\text{ }\mu\text{g/kg/min}$ or any dose of noradrenaline); neurological (impaired consciousness); respiratory ($\text{PaO}_2/\text{FiO}_2 < 300$); renal (oliguria, creatinine $>2.0\text{ mg/dL}$); hepatic (INR >1.5); haematological (platelets $<100,000/\text{mm}^3$). Biliary drainage as an immediate emergency, under volume and vasopressor support
Grade II (moderate)	Any two of: white cell count $>12,000/\text{mm}^3$ or $<4,000/\text{mm}^3$; fever $\geq 39^{\circ}\text{C}$; age ≥ 75 years; total bilirubin $\geq 5\text{ mg/dL}$; hypoalbuminaemia ($<0.7 \times \text{LLN}$) ^a . Early biliary drainage
Grade I (mild)	Does not meet the criteria for grade II or III. Initial medical treatment; biliary drainage in the absence of a response within the first 24 hours

^a The original TG18 criterion is expressed as $<\text{STD} \times 0.7$, where STD denotes the lower limit of the normal laboratory value and not an absolute albumin concentration. For a usual reference interval with a lower limit of 3.5 g/dL , the threshold corresponds to an albumin concentration below approximately 2.45 g/dL . The value is recalculated according to the reference interval of the local laboratory.

Abbreviations: ALP – alkaline phosphatase; ALT – alanine aminotransferase; AST – aspartate aminotransferase; CRP – C-reactive protein; GGT – gamma-glutamyl transpeptidase; INR – international normalised ratio; LLN – lower limit of normal; TG – Tokyo Guidelines; ULN – upper limit of normal. Source: adapted from Kiriya et al. [20] and Miura et al. [17].

adverse event rate of 6–15% [5, 22]. The stratification criteria are given in Table 2, and the performance of the imaging methods in Table 3.

Operative risk is quantified by the American Society of Anesthesiologists (ASA) class, by the Charlson comorbidity index [26] and by the POSSUM and Portsmouth-POSSUM (P-POSSUM) scores [27]. In the patient at increased surgical risk (ASA III–IV, Charlson index >2 , high estimated P-POSSUM mortality), endoscopic clearance of the bile duct is preferred, with deferral of cholecystectomy. The evidence behind this expectant strategy is fragile. A meta-analysis of 13 studies, with 2,598 patients, shows that patients who underwent cholecystectomy after endoscopic clearance had a lower risk of cholecystitis (OR 0.15; 95% CI: 0.07–0.36), of cholangitis (OR 0.51; 95% CI: 0.26–1.00, at the threshold of significance) and of death (OR 0.38; 95% CI: 0.16–0.90) [28]. Abstention from cholecystectomy remains an exception, justified by prohibitive operative risk. In the fit patient, the single-stage approach may be preferred.

The contemporary therapeutic armamentarium

Biological optimisation

Biological stabilisation precedes any attempt at invasive decompression. It requires volume resuscitation and empirical antibiotic therapy directed at gram-negative and anaerobic flora, with adequate biliary penetration; coagulopathy is corrected with vitamin K [17, 29]. In cholestasis, fat malabsorption impairs the intestinal absorption of vitamin

K, so that the enteral route cannot be relied upon when correction is required before an invasive procedure; the route intended here is slow intravenous injection. In the patient with coagulopathy the intramuscular route is avoided, because of the risk of haematoma. No randomised study has addressed the route of administration in cholestasis-associated coagulopathy. The only randomised data on route come from the reversal of anticoagulation with vitamin K antagonists, where subcutaneous administration corrected the international normalised ratio more slowly than the oral route [30]. The practice described here therefore rests on the pharmacology of absorption in cholestasis and not on direct comparative evidence.

TG18 recommends the prompt initiation of antibiotic therapy. The regimen is reassessed according to the bile cultures taken during drainage and according to local resistance profiles [29].

The national clinical protocol of the Republic of Moldova records bactibilia in 30–70% of patients with acute cholecystitis and in 20–50% of those with chronic forms. Enterobacteria (*Klebsiella* spp., *Enterobacter* spp.) and *Enterococcus* spp. predominate, alongside anaerobic flora, with *Bacteroides fragilis* as the reference species [31].

The national surveillance data impose caution on the choice of the empirical regimen. Of 99 *Klebsiella pneumoniae* strains collected between 2020 and 2023 in nine hospital laboratories, 98% were resistant to third-generation cephalosporins, 97%

Table 2. Stratification of the risk of choledocholithiasis according to the ASGE 2019 criteria

Risk category	Criteria	Management
High	Stone visualised in the CBD on ultrasonography or cross-sectional imaging; or clinically manifest acute cholangitis; or total bilirubin >4 mg/dL together with a dilated CBD	Direct ERCP, with therapeutic intent
Intermediate	Abnormal liver tests; age >55 years; dilated CBD on ultrasonography or cross-sectional imaging	Endoscopic ultrasonography or magnetic resonance cholangiopancreatography; alternatively, intraoperative cholangiography or laparoscopic ultrasonography
Low	Absence of predictive criteria	Cholecystectomy without further investigation

Abbreviations: ASGE – American Society for Gastrointestinal Endoscopy; CBD – common bile duct; ERCP – endoscopic retrograde cholangiopancreatography. Source: adapted from Buxbaum et al. [5].

Table 3. Comparative performance of imaging methods in the diagnosis of choledocholithiasis

Imaging method	Sensitivity (95% CI)	Specificity (95% CI)	Comments
Transabdominal ultrasonography	0.73 (0.44–0.90)	0.91 (0.84–0.95)	First line, by availability and cost; studies of low methodological quality
Magnetic resonance cholangiopancreatography	0.87 (0.80–0.93)	0.92 (0.87–0.96)	Non-invasive standard; reduced accuracy for microlithiasis (<5 mm)
Endoscopic ultrasonography	0.97 (0.91–0.99)	0.90 (0.83–0.94)	Sensitivity superior to magnetic resonance cholangiopancreatography; allows immediate conversion to ERCP

ERCP – endoscopic retrograde cholangiopancreatography. The values for magnetic resonance cholangiopancreatography and endoscopic ultrasonography come from a meta-analysis of head-to-head studies in the same patients (5 studies, 272 patients), in which the diagnostic odds ratio was higher for endoscopic ultrasonography (162.5 versus 79.0; $p = 0.008$), the difference arising from sensitivity [23]. The values for transabdominal ultrasonography come from a Cochrane meta-analysis [24]. Parentheses indicate the 95% confidence interval. The Cochrane meta-analysis devoted to the comparison between endoscopic ultrasonography and magnetic resonance cholangiopancreatography reports concordant values for endoscopic ultrasonography (sensitivity 0.95; specificity 0.97) [25].

to fluoroquinolones, 95% to aminoglycosides and 68% to carbapenems [32]. These figures nonetheless require careful reading: the isolates were selected for suspicion of extended-spectrum beta-lactamases or carbapenemases and come from blood and urine cultures, so that the overall prevalence of resistance is different. National data from bile cultures are lacking. Under these conditions, therapy is adjusted according to the bile collected during drainage and according to the department's own antibiogram. One measure follows from this gap. TG18 asks for bile to be cultured at the start of every biliary procedure, and for common duct bile in every case of suspected cholangitis [29]. Applied consistently, the requirement turns each drainage into a recorded observation and would, over a few years, build the national bile-culture series that empirical prescribing now lacks. Its implementation also requires microbiology processing, reporting and follow-up, so the local resource requirement extends beyond the culture bottle itself.

The endoscopic component

ERCP is the first-line intervention for decompression of the biliary tree and for ductal clearance of the CBD. ESGE recommends stone extraction in all patients with CBD stones

who tolerate the procedure; the reference technique remains ERCP with sphincterotomy [22]. By the endoscopic route, the septic source is controlled rapidly, without prolonged general anaesthesia and without insult to the abdominal wall in the acute phase.

Selective cannulation of the bile duct carries most of the iatrogenic risk. It fails in 5–15% of procedures, high-volume centres included. ESGE defines difficult cannulation by more than five contacts with the papilla, by more than five minutes of attempts or by more than one unintended cannulation of the pancreatic duct [33]. The definition has operational value, since repeated and prolonged attempts are the dominant risk factor for post-procedural pancreatitis.

Among the anatomical variants, the juxtapapillary diverticulum is the most frequent. Its effect depends on the relationship between papilla and diverticulum. The Swedish national registry (66,974 consecutive procedures, 2006–2021) identified periapillary diverticula in 12.1% of cases. With an intradiverticular papilla (Boix type 1) the rate of successful cannulation was 80.1%, compared with 88.7% in the absence of a diverticulum (OR 0.42; 95% CI: 0.38–0.46); types 2 and 3 did not differ, and adverse events and post-ERCP

pancreatitis were not increased [34]. The technical obstacle therefore relates to the intradiverticular position of the papilla. Juxtapapillary diverticula are at the same time associated with an increased incidence and recurrence of choledocholithiasis [35, 36], which justifies surveillance after ductal clearance.

Access is also complicated by periampullary inflammation or by an impacted stone. Here the difficulty is often transient, and a short delay under medical treatment may be preferable. A second situation is surgically altered anatomy — Billroth II, Roux-en-Y reconstructions, pancreaticoduodenectomy — which requires balloon-assisted enteroscopy or alternative solutions available in specialised centres.

When access proves difficult, the first obligation is to recognise the difficulty early and to abandon standard cannulation once the thresholds mentioned are reached. Ordered technical escalation follows: the double-guidewire technique, transpancreatic sphincterotomy or precut. In patients with a bile duct dilated up to the papilla, ESGE prefers needle-knife fistulotomy; when pancreatic cannulation is readily obtained, a small-calibre pancreatic stent guides the incision and lowers the risk of pancreatitis [33]. Precut, however, carries an increased risk of duodenal perforation. The decision to stop remains, with referral to rendezvous or to endoscopic ultrasound-guided biliary drainage [37], to percutaneous transhepatic drainage, to repetition of the procedure by a more experienced operator or to surgical escalation. A department without access to interventional endoscopic ultrasonography sets its threshold for surgical escalation earlier than do algorithms designed for fully equipped centres.

For large stones, limited sphincterotomy combined with endoscopic papillary large balloon dilation (EPLBD) reduces recourse to mechanical lithotripsy [38] and may reduce complications compared with extended sphincterotomy alone [22]. Mechanical lithotripsy prolongs the procedure and raises the cost of consumables.

Impacted or refractory stones benefit from cholangioscopy-assisted intraductal lithotripsy, electrohydraulic or laser: rates of ductal clearance are high and the safety profile is acceptable [39].

Prophylaxis of post-ERCP pancreatitis depends on guidewire-assisted selective cannulation and on rectal administration of non-steroidal anti-inflammatory drugs (NSAIDs); in patients at risk a pancreatic stent is placed prophylactically [33]. In the multicentre randomised trial of Elmunzer et al., rectal indomethacin lowered the incidence of post-ERCP pancreatitis from 16.9% to 9.2% in high-risk patients [40].

TG18 prefers endoscopic transpapillary biliary drainage to percutaneous transhepatic or surgical drainage, for its lower complication rate [41]. When ERCP fails, the alternative is endoscopic ultrasound-guided drainage — hepaticogastrostomy, choledochoduodenostomy, rendezvous — which nonetheless requires expertise and dedicated material [37]. The order in which the alternatives are considered changes with the resources of the department. Endoscopic

ultrasound-guided drainage needs dedicated stents, an operator trained in the technique and the means to manage its specific complications, and ESGE places it in expert centres [37]. Where those conditions are absent, percutaneous transhepatic drainage remains the realistic second line, and TG18 accepts it as such [41]. The decision belongs in the written protocol of the department, settled before the case arrives.

The laparoscopic component

Safe laparoscopic cholecystectomy requires the critical view of safety (CVS) described by Strasberg: the cystic duct and the cystic artery are identified unequivocally before any division [42]. In cases with severe inflammation, the multi-society Safe Cholecystectomy guideline recommends subtotal cholecystectomy, as a manoeuvre that avoids iatrogenic biliary injury [43]. The manoeuvre has its own price, recorded in the same guideline. Bile leak occurred in 27.8% of the pooled cases and retained stones in 3.1%. In one retrospective multicentre comparison reported by the same guideline, subtotal cholecystectomy, compared with conversion to open total cholecystectomy, was associated with more recurrent biliary events (15% versus 3%), more readmissions (18% versus 8%) and more reinterventions (34% versus 18%) [43]. The bile duct is protected during the operation, and part of the risk moves to the follow-up period, which has to be planned accordingly.

Intraoperative cholangiography and laparoscopic ultrasonography detect unsuspected choledocholithiasis and clarify the anatomy. Laparoscopic exploration of the CBD follows the transcystic route for small and few stones, and the transcholedochal route for large or multiple stones. The transcholedochal approach achieves superior ductal clearance, at the price of longer operative time and hospital stay [44].

A meta-analysis updated in 2025 compared primary closure of the choledochotomy with T-tube drainage. Primary closure was associated with fewer retained stones (OR 0.57; 95% CI: 0.35–0.93) and less biliary peritonitis (OR 0.22; 95% CI: 0.08–0.60), with shorter operative time (mean difference –21.1 minutes) and shorter postoperative stay (mean difference –2.2 days). Stone recurrence, biliary fistula, bile duct stricture and pancreatitis did not differ significantly [45]. The results agree with earlier meta-analyses [46] and support abandoning the routine T-tube in selected patients.

Open surgery and biliary-enteric reconstruction

The open approach remains indispensable when minimally invasive clearance fails, as well as in complex intrahepatic lithiasis, in Mirizzi syndrome types III–IV, in extensive benign biliary strictures and in major iatrogenic biliary injuries. The reference reconstructive solution is Roux-en-Y hepaticojejunostomy. Its long-term results depend on intraoperative recognition of the injury and on a repair undertaken by a hepatobiliary surgeon in a tertiary centre [7, 47].

In the Republic of Moldova, the research devoted to benign biliary strictures analysed a separate series of 203 cases treated in the Department of Surgery no. 2 between

1998 and 2015. High Bismuth II (45.3%) and III (44.3%) forms predominated [48]. Hepaticojejunal anastomosis by continuous single-layer suture, with temporary external drainage, gave a more watertight anastomotic line and fewer early bile leaks than interrupted sutures [48].

Sequential and multimodal therapeutic strategies

The most frequently applied algorithm in choledocholithiasis associated with gallbladder stones remains the two-stage approach: ERCP with sphincterotomy, then laparoscopic cholecystectomy. The preference is explained where endoscopic expertise is more widely available than advanced laparoscopic biliary surgery [22].

Randomised studies comparing early cholecystectomy (≤ 72 hours) with delayed cholecystectomy (> 72 hours) after ERCP have been pooled in a meta-analysis, and the result supports a shorter interval than that practised at present. With moderate certainty, the early approach reduces conversion to open surgery (RR 0.35; 95% CI: 0.17–0.68) and recurrent biliary events (RR 0.09; 95% CI: 0.03–0.28). Operative time (mean difference –17.6 minutes), postoperative complications (RR 0.46; 95% CI: 0.26–0.82) and length of stay also appear lower [49].

The biliary stent placed as a bridge to delayed cholecystectomy has no support. The meta-analysis devoted to it found no benefit on the recurrence of symptoms (OR 0.74; 95% CI: 0.30–1.79) nor on adverse events [50].

The single-stage approach is addressed to stable patients, selected electively, with favourable anatomy; it uses laparoscopic exploration of the CBD combined with cholecystectomy or the laparoendoscopic rendezvous technique (LERV) [51, 52]. In LERV, the endoscopist retrieves the guidewire placed antegradely through the cystic duct during cholecystectomy and uses it for sphincterotomy and stone extraction. Repeated attempts on the papilla are thereby avoided, and the risk of post-ERCP pancreatitis falls [51]. Table 4 summarises the comparison of the two strategies.

The Cochrane review comparing surgical with endoscopic treatment of CBD stones found no significant differences in

morbidity and mortality between laparoscopic and endoscopic clearance; the choice remains a matter of local expertise, available resources and patient preference [6]. A second Cochrane review, devoted to the rendezvous technique, analysed five randomised studies with 517 participants. The greatest certainty concerns operative time, which was shorter in favour of preoperative endoscopic sphincterotomy; for mortality, morbidity and ductal clearance, the quality of the evidence is low [53]. Meta-analyses comparing the single-stage with the two-stage approach report similar rates of ductal clearance, the former having an advantage in length of stay and in the number of procedures [52, 54].

Well-organised sequential protocols can reduce conversion and perioperative morbidity, and hospital stay is shortened. The effect is more visible when they are integrated into enhanced recovery programmes, for which dedicated recommendations exist for hepatobiliary surgery [55].

Quality of life and long-term outcomes

In benign biliary disease, patient-reported quality of life has become a criterion of success. Among the internationally validated instruments, the generic SF-36 questionnaire and the EQ-5D utility index are used, alongside the Gastrointestinal Quality of Life Index (GIQLI), with 36 digestive-specific items [56]. The national case material has used the Gastrointestinal Symptom Rating Scale (GSRS), in combination with SF-36 [48].

Major complications, iatrogenic biliary injury first among them, affect the functional result durably. A cohort of 800 patients referred to a tertiary centre after bile duct injury had a mean survival of 17.6 years and a mortality attributable to the injury of 3.5%; quality of life and working capacity remained below those of patients with uncomplicated cholecystectomy [57]. The Swedish national study confirms the lasting impairment of SF-36 scores after repair by hepaticojejunostomy [58]. In major injuries of Strasberg type E, long-term patency is better when the initial repair is undertaken by a hepatobiliary surgeon [47].

The national case material assessed the long-term results

Table 4. Comparison of therapeutic strategies in choledocholithiasis associated with gallbladder stones

Parameter	Two-stage approach	Single-stage approach
Ductal clearance	High	Comparable
Number of anaesthetics	Two	One
Total length of hospital stay	Longer	Shorter
Operative time of the laparoscopic procedure	Shorter	Longer for LERV
Post-ERCP pancreatitis	Risk maintained	Reduced in the rendezvous variant
Organisational requirements	Low; sequential, in separate departments	High: mixed team, hybrid theatre, coordination within the same session
Mortality	No demonstrated difference	No demonstrated difference

Abbreviations: ERCP – endoscopic retrograde cholangiopancreatography; LERV – laparoendoscopic rendezvous technique. Source: synthesis after references [22, 45, 51–54].

of hepaticojejunal anastomoses by the Terblanche score, in 97 patients: group I – 34 (35.1%), group II – 28 (28.9%), group III – 12 (12.4%) and group IV – 23 (23.7%). The last group comprises recurrent strictures and significant hepatobiliary dysfunction. The SF-36 and GSRS questionnaires documented the advantage of the continuous suture anastomosis [48].

Discussion

International protocols converge on general principles and diverge at the thresholds for action. For a system with intermediate resources, the divergences are the informative part: they mark the areas where the decision legitimately remains local.

Areas of convergence

The documents analysed support four principles concordantly. Graded severity of cholangitis determines the timing of drainage (the Tokyo Guidelines [17, 20] and the ASGE cholangitis guideline [18]). Purely diagnostic ERCP is to be avoided (ASGE [5], ESGE [22] and the updated British guideline [59]). The critical view of safety and subtotal cholecystectomy remain the bail-out manoeuvres in severe inflammation (the multi-society guideline [43] and the WSES recommendations on bile duct injury [7]). Endoscopic transpapillary drainage is preferred to the percutaneous route (TG18 [41] and ESGE [22]). Two of these four principles — the timing of drainage and the preference for the transpapillary route — presuppose an endoscopy service with fluoroscopy and appropriate expertise. In centres where this infrastructure and this expertise are available, their implementation depends mainly on the organisation of the patient pathway.

The real power of the stratification criteria

External validation shows an accuracy lower than the ASGE and ESGE criteria would suggest. A retrospective study of 521 patients, from a population with a high prevalence of choledocholithiasis (61.0%), found in the high-risk group a positive predictive value of 73.6% for the ASGE criteria and of 73.7% for the ESGE criteria. The positive likelihood ratios were 1.78 and 1.79 respectively, while 69.7% and 65.6% of patients respectively were classified as high risk [60].

A systematic review with meta-analysis reaches the same conclusion. The principal strength of the criteria lies in ruling out choledocholithiasis in low-risk patients, who may proceed directly to cholecystectomy. Specificity for high risk remains limited, and selection for first-intention ERCP is not reliable [61]. The SAGES criteria gave similar results [62].

In case material marked by late presentation, the proportion of high-risk patients is predictably large. Applied mechanically, stratification would here produce ERCPs without therapeutic purpose and the iatrogenic morbidity that accompanies them [5]. Confirmation by magnetic resonance cholangiopancreatography or endoscopic ultrasonography retains its usefulness in a proportion of patients formally classified as high risk as well, provided it does not delay decompression. Clinically manifest cholangitis

is the exception.

The divergence concerning intraoperative cholangiography

For elective cholecystectomy, the 2020 multi-society guideline abstained from a recommendation on cholangiography and suggested only its liberal use in acute cholecystitis (conditional recommendation, very low certainty) [43]. The SAGES guideline devoted to intraoperative imaging is more explicit. It makes conditional recommendations in favour of routine over selective cholangiography and over indocyanine green fluorescence, and it considers laparoscopic ultrasonography equivalent [63].

The two guidelines work with the same data and set different thresholds for action under uncertainty. A synthesis of 14 studies, with about 2.5 million patients, shows that the majority of adjusted estimates favoured cholangiography, with maximum benefit in acute cholecystitis. In patients with an intraoperatively suspected biliary injury, cholangiography increased almost threefold the chance of recognising the injury [43, 63].

The functional prognosis after biliary injury depends first on the moment of recognition, then on the specialisation of the team that performs the repair [47, 48, 57, 58]. In a system in which referral to a tertiary centre may be delayed, the argument for the wide use of intraoperative cholangiography becomes stronger.

The choice between the single-stage and the two-stage approach

The reference guidelines leave this choice open. ESGE formulates recommendations on sequence and interval without imposing a single algorithm [22], and the Cochrane synthesis refers the decision to local expertise, resources and patient preference [6]. In practice, the choice appears to depend mainly on organisational variables: the simultaneous availability of the surgeon and the endoscopist, the equipment of the operating theatre, the coordination of the operating list. Patient characteristics intervene only secondarily.

Synthesis of the high-level evidence and the desiderata that follow from it

From the comparison of high-level syntheses, verifiable practical desiderata follow, which may become quality indicators at departmental level. Table 5 sets them out.

Where an endoscopy service with fluoroscopy and trained operators is already in place, the desiderata with the largest demonstrated effect — drainage within the first 48 hours, rectal NSAIDs, primary closure of the choledochotomy in selected patients, cholecystectomy during the same admission — depend mainly on organisation. What is required is a biliary emergency pathway and a written protocol, together with an operating list that reserves capacity for patients already admitted. As a pragmatic minimum data set proposed here, the fields needed to use these desiderata as indicators are few: the date and hour of admission, the date and hour of drainage, the severity grade at admission, whether a rectal NSAID was given before ERCP, and the interval between endoscopic clearance and cholecystectomy. Five fields, recorded prospectively, show

Table 5. *Reference syntheses and the practical desiderata that follow from them*

Decision domain	Reference synthesis	Key result	Practical desideratum
Timing of drainage in acute cholangitis	Meta-analysis, 9 studies, 7,534 patients [21]	Drainage ≤ 48 h: in-hospital mortality OR 0.52; hospital stay -5.6 days	Institutional threshold of 48 h; admission-to-drainage interval recorded as a quality indicator
Stratification of the probability of choledocholithiasis	Systematic review with meta-analysis [61]	The strength of the criteria lies in ruling out low risk; limited specificity at high risk	Criteria used to spare low-risk patients further investigation
Choice of imaging method	Head-to-head meta-analysis [23]	Overall accuracy in favour of endoscopic ultrasonography, particularly for small stones	Method chosen according to the size of the suspected stone
Prophylaxis of post-ERCP pancreatitis	Multicentre randomised trial [40]	Rectal indomethacin: incidence from 16.9% to 9.2%	Rectal NSAID in eligible patients, in the absence of contraindications
Large stones	Systematic review with meta-analysis [38]	EPLBD reduces the need for mechanical lithotripsy	EPLBD may be used before mechanical lithotripsy for large stones, according to clinical indication
Refractory stones	Systematic review with meta-analysis [39]	Cholangioscopic lithotripsy achieves high ductal clearance	Objective criterion for referral to a centre with cholangioscopy
Route of laparoscopic exploration	Meta-analysis [44]	Transcholedochal approach: superior clearance, longer hospital stay	Transcystic for small stones; transcholedochal for large or multiple stones
Closure of the choledochotomy	Updated meta-analysis [45]	Retained stones OR 0.57; biliary peritonitis OR 0.22; -2.2 days of hospital stay	Primary closure may be preferred in selected patients; T-tube on individualised indication
Single-stage versus two-stage approach	Network meta-analysis [54]; meta-analysis with trial sequential analysis [52]	Comparable rates of ductal clearance	The choice documented as an organisational decision
Rendezvous technique	Cochrane review, 5 studies, 517 patients [53]	Statistical certainty only for operative time, against LERV	To be evaluated prospectively where it is practised
Timing of cholecystectomy after ERCP	Meta-analysis of randomised trials [49]	≤ 72 h: conversion RR 0.35; recurrent biliary events RR 0.09	Cholecystectomy during the same admission
Cholecystectomy versus abstention	Meta-analysis, 13 studies, 2,598 patients [28]	Cholecystitis OR 0.15; cholangitis OR 0.51; mortality OR 0.38	Cholecystectomy is recommended in the absence of prohibitive operative risk; abstention requires justification
Biliary stent while awaiting surgery	Systematic review with meta-analysis [50]	No benefit on the recurrence of symptoms (OR 0.74)	Not placed routinely; the waiting interval is shortened instead
Prevention of biliary injury	Multi-society guideline [43]; guideline devoted to imaging [63]	Cholangiography triples the chance of recognising a suspected injury	At least liberal use, with a threshold that is lower the slower tertiary referral is

Abbreviations: EPLBD – endoscopic papillary large balloon dilation; ERCP – endoscopic retrograde cholangiopancreatography; LERV – laparoendoscopic rendezvous technique; NSAID – non-steroidal anti-inflammatory drug; OR – odds ratio; RR – risk ratio.

a department where it stands and allow it to measure whether a change in the pathway has produced an effect.

Some desiderata contradict widely established practices. Systematic postponement of cholecystectomy by two weeks or more, the biliary stent placed as a safety measure during the waiting period and the implicit abstention from cholecystectomy in the elderly patient with a cleared bile duct remain weakly supported by the evidence analysed.

Within the range of procedures a department already performs, the following can be applied without significant additional cost: TG18 triage, the criteria that exclude low lithiasic risk, the critical view of safety and subtotal cholecystectomy, primary closure of the choledochotomy, prophylaxis with rectal NSAIDs and the adaptation of empirical antibiotic therapy to the local microbial ecology. Diagnostic and interventional endoscopic ultrasonography, cholangioscopy, the hybrid theatre and structured enhanced recovery programmes require investment and a learning curve.

Limitations of the synthesis

The work is a structured narrative review. No prospective protocol was registered, selection did not follow a PRISMA flow diagram, and risk of bias was not formally assessed; the weight given to sources therefore also reflects the judgement of the authors.

Most of the high-level evidence comes from high-volume centres, which limits its transfer to departments with reduced resources. Heterogeneous definitions of the difficult stone, of complete clearance and of technical success hinder comparisons. A desideratum derived from observational studies, such as the 48-hour threshold, has less force than one derived from randomised trials. Data on quality of life come predominantly from Western European and North American cohorts. In the Republic of Moldova the SF-36 and GSRS questionnaires have been used [48]; an instrument specific to digestive disease such as the GIQLI still awaits linguistic and cultural validation.

Perspectives

Consensus definitions and minimum reporting sets for the difficult stone and for complete clearance remain a priority. To these are added the evaluation of single-use cholangioscopy and of endoscopic ultrasound-guided drainage in systems with limited resources, as well as validation of the ERAS

recommendations for common bile duct exploration.

The surgical school of Chisinau has substantial case material in benign biliary obstruction and in the reconstructive surgery of strictures [1, 2, 8, 9, 48, 64]. Extending this base towards the minimally invasive segment is the immediate priority: documented rates of ERCP failure, predictors of surgical escalation, microbial profile of bile. The validation of instruments for the assessment of quality of life belongs to the same programme.

Conclusions

Benign obstructive jaundice is an aetiologically heterogeneous entity, dominated by choledocholithiasis. Management depends on an understanding of the pathophysiology of cholestasis, on rigorous clinical and biological triage and on dynamic stratification of operative risk.

Treatment has moved from emergency open surgery towards individualised multimodal strategies. The endoscopic component, the laparoscopic component and open surgery are integrated sequentially or in hybrid fashion, according to the biological status of the patient, the severity of cholangitis, the probability of choledocholithiasis and the operative risk.

The sequential two-stage approach and the single-stage approach achieve comparable rates of ductal clearance. The choice between them depends on the expertise available, on institutional organisation and on the informed preference of the patient. In selected patients, when the technical conditions are met, primary closure of the choledochotomy may be preferred to routine T-tube drainage. Prevention of iatrogenic biliary injury remains the objective with the greatest effect on long-term functional prognosis.

The desiderata with the best demonstrated effect are four: biliary drainage within the first 48 hours in acute cholangitis, prophylaxis of post-ERCP pancreatitis with rectal NSAIDs, primary closure of the choledochotomy in selected patients and cholecystectomy performed during the same admission after endoscopic clearance. Three of them presuppose an endoscopy service with fluoroscopy and trained operators. Where this is available, all four depend on the reorganisation of the patient pathway rather than on additional equipment.

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