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**Modern approach to cholecysto-choledocholithiasis**

Bencini L et al. Cholecysto-choledocholithiasis

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**Abstract**

Gallstones and common bile duct calculi are found to be associated in 8%-20% of patients, leading to possible life-threatening complications, such as acute biliary pancreatitis, jaundice and cholangitis. The gold standard of care for gallbladder calculi and isolated common bile duct stones is represented by laparoscopic cholecystectomy and endoscopic retrograde cholangiopancreatography, respectively, while a debate still exists regarding how to treat the two diseases at the same time. Many therapeutic options are also available when the two conditions are associated, including many different types of treatment, which local professionals often administer. The need to limit maximum discomfort and risks for the patients, combined with the economic pressure of reducing costs and utilizing resources, favors single-step procedures. However, a multitude of data fail to strongly demonstrate the superiority of any technique (including a two or multi-step approach), while rigorous clinical trials that include so many different types of treatment are still lacking, and it is most likely unrealistic to conduct them in the future. Therefore, the choice of the best management is often led by the local presence of professional expertise and resources, rather than by a real superiority of one strategy over another.

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**Key words:** Laparoscopy; Endoscopy; Laparo-endoscopic; Endoscopic retrograde cholangiography; Bile duct stones; Cholecystolithiasis; Common bile duct stones; Laparoendoscopic rendezvous

**Core tip**: There is no consensus on the correct strategy for the care of simultaneous gallbladder and common bile duct stones. Many therapeutic options are available, including laparoscopic, endoscopic, percutaneous and open traditional techniques, either through a combination of these treatments or by conducting them in a stepwise sequence.

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**INTRODUCTION**

Common bile duct stones (CBDS) occur in 8%-20%[1,2] of patients suffering from gallstones, although actual incidences of CBDS in this patient group could be higher. The association of these two conditions can lead to many severe complications, such as acute biliary pancreatitis, jaundice and cholangitis, transforming the choice of the best strategy for treating a benign issue into a potentially life-threatening problem. Although some authors have advocated for a “wait and see” policy for asymptomatic gallbladder stones[3], almost none could propose the same approach if CBDS are detected as well[2,4]. Nonetheless, a significant paper also reported a conservative (no action) behavior for silent CBDS found during routine intraoperative cholangiogram (IOC)[5]. Moreover, in the case of patients with severe comorbidity unfit for surgery and symptoms of CBD obstruction (jaundice, cholangitis, recurrent acute pancreatitis),the sole execution of a formal endoscopic retrograde cholangiography (ERCP) is often obligatory, leaving the gallbladder in situ[6]. However, a Cochrane review failed to confirm the imperative necessity of an immediate ERCP to relieve acute pancreatitis without sepsis[7]. A very intriguing observational study from Sweden[8] reported a so-called “paradigm shift” from open choledochotomy and cholecystectomy toward bile duct clearance using the endoscopic route and selective laparoscopic cholecystectomy in patients suffering from cholecysto-choledocholithiasis (CCL).

While the “gold standard” of treatment for gallstones has been laparoscopic cholecystectomy (LC) since the early 1990s[9,10] and ERC is considered optimal for isolated CBDS[4]], no consensus exists to address CCL[11,12]. The European Association for Endoscopic Surgery published the comprehensive guidelines of minimally invasive approaches in 2006, but no robust statements were published regarding the best treatment for CCL[13].

Many therapeutic options are available, including laparoscopic, endoscopic, percutaneous and open traditional techniques, either as a combination in a concurrent manner or as a stepwise sequence.

The choice of the best strategy is often led by the local presence of professional expertise and resources, rather than by a real superiority of one strategy over another[12,14-18].

However, the current standard of treatment for CCL is influenced by many different professionals, including gastroenterologists, anesthesiologists, surgeons and endoscopists, leading to some conflict regarding organizing approaches for treatment.

We performed a Pubmed, Embase and Cochrane bibliographic search for CCL, updated in October 2013, by manually searching for interesting cross-matched references. Reporting on more recent articles, randomized clinical trials (RCTs) and meta-analyses was considered a priority. Intrahepatic bile duct stones represent a less common disease with several peculiar pathological etiologies and will not be considered further in this review. Despite some differences in the epidemiologic features of gallstones and CCL, a special effort was made to include papers published from all over the world, including North America, Europe and Asia.

**DIAGNOSIS OF COMMON BILE DUCT STONES**

The first crucial issue for correctly managing CCL is to reach a good diagnosis in order to reduce unplanned procedures, unnecessary invasive exams and under treatment. Traditionally, the gold standard of diagnosis is achieved by cholangiography, which can be conducted by means of an intraoperative route (injecting the contrast medium through the cystic or the common bile duct), by an endoscopic papillary injection or even by a percutaneous approach. All methods are, of course, invasive.

Since the advent of laparoscopy, the preoperative diagnosis of CBDS has become increasingly popular due to the need for avoiding laparoscopic IOC and further treatments that were, at the beginning of the experience, highly demanding. Moreover, the widespread adoption of ERCP, even as a diagnostic tool, enormously impacted the development of some excessively invasive algorithms due to success rates of CBD clearance of almost 98% in the hands of experienced endoscopists[19].

Currently, IOC is routinely performed in some centers[20-22] and selectively in others[23,24], while it is easily reproducible by the majority of surgeons. Nevertheless, the definitive acceptance of one policy over another has not been confirmed[25], with selective IOC having some advantages in terms of a shorter operating time and fewer perioperative complications but at the price ofa higher readmission rate if CBDS are subsequently detected[22]. Moreover, laparoscopic CBD exploration is becoming more popular, while intraoperative or postoperative ERCP is also safe and effective. However, current good practice should reserve the use of ERCP for those patients with CBDS as a therapeutic strategy only in selected doubtful cases[18] due to the possibility of complications[26-28] and false-positives.

Many of the diagnostic flow-charts and algorithms proposed consider a baseline stratification of the risk of having CBDS, including ultrasonography dilatation of the CBD and biochemical parameters, such as gamma-glutamyl transpeptidase, transaminases, alkaline phosphatase, bilirubin and lactatedehydrogenase. All of these markers are combined in predictive models[16,29] to reserve more invasive or expensive imaging - cholangiography by ERCP or IOC, magnetic resonance cholangiography (MRC) and endoscopic ultrasonography (EUS) - for higher-risk patients, although no clinical-laboratory parameter is able to predict CBDS with optimal accuracy[30].

Currently, the most importantpreoperative diagnostic tools are MRC and the traditional ultrasound[31-35]. Alternatively, the policy of routine MRC was not found to be cost-effective in patients without symptoms or suspicion of CBDS, whereas IOC during LC was the best strategy[36]. Interestingly, some authors reported[37] the routine use of IOC during LC, even after MRC and successful preoperative ERCP, to detect residual CBDS. Indeed, due to the higher sensibility of IOC over MRC, it could be hypothesized that there is no need to conduct preoperative MRC in those patients suspected to have CBDS who are already scheduled for an intervention[38].

Recently, introducing EUS added a new tool to the diagnostic algorithm of CDS. Despite the relatively scarce use of this technique among many hospitals worldwide, its routine use, at least in patients with intermediate and high risk of CBDS[39-42], could play an important role for the next future two-stage strategy. A proposed rational sequence could reserve EUS for those patients with intermediate to high risk of CBDS and a negative MRC[43]. A realistic and intriguing new proposal could consider the adoption of EUS in selected patients suspected to have CBDS, followed by a consecutive session of ERCP[44].

The role of the CT scan in detecting CBDS is quite marginal, and its use is limited by the low frequency of radiopaque stones and cut-off size[45]. However, it may be useful when a silent incidental stone is found.

**CCL**

There are many options to treat CCL, but each one has different advantages and limitations. Few trials have demonstrated robust evidence of one method’s superiority over another. The local availability of both technical resources and professional expertise could also play a pivotal role in deciding which treatment to administer.

**Open surgery**

From a historical point of view, CBD exploration has been performed at the same time as a cholecystectomy by open choledochotomy with papillotomy and stone extraction, often with a T-Tube placement, with an unacceptable morbidity and mortality[11,46]. Therefore, it was proposed to abandon this method on a routine basis 20 years ago[47]. A more recent retrospective series reported good results with primary closure of choledochotomy where endoscopic and minimally invasive facilities are not available[48]. Currently, open choledochotomy and papillotomy could still play a role in those cases with intraoperative unexpected diagnosis of choledocholithiasis and cholangitis, with bile duct dilatation or where all other endoscopic, percutaneous and laparoscopic approaches failed. Open choledochotomy and papillotomy could also be used in the case of a pre-existing open surgery that limits the application of endoscopic approaches (i.e., Roux-en-Y intestinal reconstruction after gastrectomy)[11].

**Preoperative ERCP (and sub-sequential laparoscopic cholecystectomy)**

A CBD clearance can be carried outby ERCP with endoscopic sphincterotomy (ES) before LC in many cases, and it is most likely the most common strategy used in the majority of hospitals worldwide[4]. As previously reported, due to its intrinsic invasiveness, ERCP should be proposed for those patients with confirmed bile duct stones only. Furthermore, there is the possibility of some increased difficulty when performing LC after an endoscopic procedure[49]. Thus, this two-stage strategy raises the problem of a close sequence of pre-endoscopic imaging through conventional US, MRC or EUS and a following LC within a maximum of 72 h that, practically, leads to some organizational problems in a busy hospital setting. The other drawback of any two-stageprocedure is that the patient undergoes two different uncomfortable anesthesiologic sessions.

**Postoperative ERCP (after laparoscopic cholecystectomy)**

In those patients with a lower risk of CBDS, a policy of selective IOC and ERCP after LC seems to be rational[50]. Similar situations are represented by intraoperative diagnosis of CBDS when an endoscopist or a surgeon trained to perform a laparoscopic bile duct clearance is not available in the operating theatre or in those cases of misdiagnosed CBDS discoveredonly after LC. Obviously, two anesthesiologic sessions are needed, which are likely to disturb the patient. Lastly, the main risk of such an approach is to fail a complete bile duct clearance postoperatively and to then haveto conduct further procedures[51].

**Intraoperative ERCP (with concomitant laparoscopic cholecystectomy)**

The single-stage laparoendoscopic treatment, known as the “Rendez-vous Technique” (RVT), is used to indicate simultaneous LC and intraoperative ERCP, facilitated by papilla visualization and cannulation through a guide-wire the surgeon inserts into the cystic duct. The technique was first described almost 20 years ago[52-54], and hypothetically, it combines many advantages, such as minimal invasiveness and an acceptable learning curve, at the price of some organization troubles between endoscopists, surgeons and operating room personnel[55-57], but is yet to be accepted. A robust review by La Greca et al[58] analyzed data from 27 papers, which included almost 800 patients and compared the RVT to other approaches. This research showed an overall bile duct clearance of 92.3% and few complications (1.6%-6% bleeding from the sphincterotomy and 1.7%-7% pancreatitis). These advantages are related to the use of a guide wire that allows a facilitatedcannulation of the papilla without the risk of irritating the pancreatic duct.

The initial drawback of the endoscopic step completed in the supine position of the patient has not been confirmed[59]. Many experiences were reported in the literature[60-63], confirming safety, excellent CBD clearance percentages, and short learning curves. The adjunct of the intraoperative procedure does not prolong hospitalization of routine LC[64].

**Concomitant laparoscopic cholecystectomy and common bile duct exploration**

One possible exciting and rational option to address CCL is conducting laparoscopic CBD exploration (LCBDE) during routine LC[65]. In this case, the surgeon is able to resolve the patient’s disease completely during the same session, avoiding the risks of sphincterotomy[26] and withoutthe need to conduct further treatments. Additionally, the abovementioned preoperative step of diagnosis could be outdated (an IOC is mandatory before LCBDE). Some surgeons with sufficient expertise in advanced laparoscopy have proposed LCBD as an excellent option for CCL[66,67], but acceptance of such a technique in most hospitals is far off due to its steep learning curve, especially when a T-tube has to be used[68].

Moreover, the surgeon’s experience influences the choice of technical procedure, such as the extraction of stones by the transcystic route[69] rather than performing a choledochotomy or the decision to do primary closure versus T-tube placement [70].

None of these differences, however, impacted the patients’ final outcomes. One of the most challenging maneuvers during LCBDE is the placement of a T-tube after closing the choledochotomy, but the real advantages, in terms of postoperative morbidity, of such a procedure are not confirmed according to a recent review article and meta-analysis[71].

**Shifts between the approaches and other techniques**

The spectrum of variability of the different approaches is prone to some percentage of failure. Notwithstanding these limitations, almost each of these techniques can be used if one does not work, raising the overall success rates. For example, the RVT could be attempted inthe case of uncompleted preoperative ERCP caused by a difficult papillary approach[72]. Alternatively, if the guide-wire insertion through the cystic duct during the RVT is not possible, a skilled endoscopist is able to complete the one-stage procedure through a conventional intraoperative ERCP[57]. Moreover, a failed preoperative or intraoperative ERCP could lead to an LCBDE or an open intervention, while a second-look at a multiple-session ERCP (often with stenting) is always possible with the help of shock-wave technologies or percutaneous trans-hepatic treatments[73-75].

**COMPARING THE DIFFERENT TECHNIQUES**

In times of reduced resources, it is of utmost importance whether the one-stage management of patients with CCL is associated with reduced costs compared with a two-stage procedure[76]. However, the economic pressure should be balanced with some learning curve to gain experience with more recent mini-invasive single-stage strategies, with the goal of similar patient outcomes. A summary of the pros and cons of each different strategy is shown in Table 1.

One of the first logical consequences of introducing ERCP in almost all hospitals was limited mass open operations, while advanced laparoscopy led to comparing the open procedure and CBD clearance with the total laparoscopic approach. LCBDE was confirmed to be superior compared to open surgery in terms of mortality and morbidity (but less effective for common bile duct clearance) since 2006[77]. Theoretically, LCBDE minimizes the risks of post-ERCP complications[26-29] and the need for further anesthesia, with an excellent success rate of stone extraction (more than 90%)[67,77]. However, LCBDE remains limited to centers with advanced laparoscopic expertise [12].

Furthermore, the high availability of ERCP in almost all hospitals limited the mass of such study designs, and the acceptance of the superiority of LC over open operation avoided further protocols. Indeed, one recent prospective trial comparing LCBDE and open surgery confirmed the superiority of the laparoscopic method in terms of efficiency, morbidity and mortality[78].

When comparing the two-stage (LC with preoperative or postoperative ERCP) and single-stage (LC with LCBDE), no significant differences were found, except for some intrinsic characteristics (fewer therapeutic sessions)[70,80]. Another trial[81] reported having a reduced hospital stay when using LCBDE.

A very recent review and meta-analysis[82] of six RCTs comparing prospectively preoperative ERCP and RVT concluded that the latter method resulted in a reduced incidence of endoscopy-related pancreatitis and a shorter hospital stay, although stone clearance and overall morbidity were almost equivalent. Another meta-analysis[83] included RVT in the so-called one-stage procedure, merging studies regarding LCBDE and comparing this group to the two-stage procedures (LC preceded or followed by ERCP). Again, no statistically detectable differences in patients’ outcomes were recorded between the two strategies.

Another review[84], conducted only by comparing two-stage procedure clearance versus RVT, found a reduced incidence of postoperative pancreatitis with the latter method (2.4% instead of 8.4; OR, 0.33; 95%CI: 0.12–0.91, P = 0.03). Another group[85]published the results of a comparative study of 200 patients, suggesting the superiority of RVT over preoperative ERCP in terms of hospital stay. In contrast, the RCT published by Rábago et al[86] reported similar percentages of CBD clearance between the two approaches. A study by Hong et al[87] compared LCDE and RVT, and no differences were found between the two groups regarding duration of surgery, success rate, complications, retained stones, hospital stay, and costs. Another study[88] also reported similar ductal stone clearance rates, although LCBDE was associated with shorter hospital costs.

The most updated and comprehensive review of available literature likely was published in 2013 by the Cochrane Group[89]. After a careful and rigorous selection, only 16 RCTs, including a total of 1758 patients, were taken into consideration. The trials compared most of the options available to treat CCL. Although the authors advised about the high risk of bias, they found no significant difference in the mortality and morbidity between open surgery versus ERCP clearance (1% vs 3%, 20% vs 19%, respectively). However, patients who received open surgery had fewer retained stones (6% vs 16%).

Again, there was no significant difference in the main outcomes between LCBDE andpre-operative ERCP. Similar results were found when comparing trials on LCBDE vs RVT or post-operative ERCP. Interestingly, there was a detectable difference in the numbers of retained stones between LCBDE and postoperative ERCP (9% vs 25%). Therefore, single-staged LCBDE vs two-staged pre-operative or post-operative ERCP appeared to lead to comparable results in terms of mortality and morbidity, with a non-significant difference in the percentage of retainedstones in the single-stage group (8% vs 14%, P = 0.94).The authors concluded that open bile duct surgery seems superior to ERCP in achieving CBDS clearance, but data referred to the early endoscopy era.

Presently, no single study comparing the whole spectrum of treatments (preoperative, postoperative ERCP, LCBDE, RVT) has been published, most likely due to the unrealistic contemporaneous presence of so many professionals and dedicated resources in the same facility. In our department, for example, there is a great availability of very skilled endoscopists (three professionals) who are able to manage intraoperative ERCP with challenging situations, while MRC needs a long time to be scheduled due to a very busy imaging service. However, it is very difficult to schedule several LC within an appropriate time after a preoperative ERCP, which is to be balanced with oncologic patients. Therefore, our approach to CCL is usually based on the RVT[57].

From a theoretic point of view, the best approach should be that in which all options are available in the same facility, modulating each one according to the single patient. Moreover, in the case of failure, other options could be proposed to guarantee a successful CCL resolution. A proposed algorithm is shown in Figure 1.

**CONCLUSION**

The current management of CBD stones associated with gallstones requires anadequate approach due to the possibility of perioperative morbidity and mortality with severe impact on the quality of life. Many strategies are available at present, mostly involving LC as a pivotal step in the entire process. The extremities of the spectrum of treatments are represented by open traditional surgery and full laparoscopic cholecystectomy with CBD clearance. However, in the majority of hospitals worldwide, ERCP is the preferred choice used to complete an LC. Timing of the ERCP (preoperative, intraoperative or postoperative) is often dictated by the local presence of professional expertise and resources, rather than by a real superiority of one method over another. However, data refer to the early spectrum of treatments, which are influenced by economic pressure to prefer single-stage management approaches.

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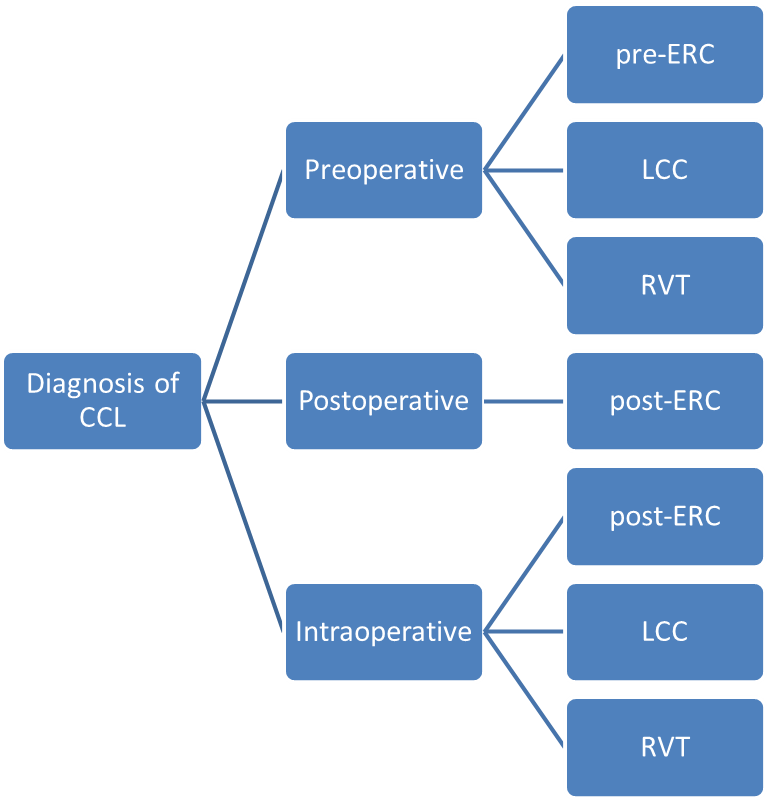
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**Figure 1 A proposed algorithm for a combined-multimodal approach to cholecysto-choledocholithiasis.** CCL: Cholecysto-choledocholithiasis; ERC: Erythropoietin-responsive cells; RVT: Rendez-vous Technique; LCC: Laparoscopic cholecystectomy.



**Intraoperative switch between the techniques**

**Repeated**

**post-ERCP**

**Open Surgery**

**Alternative treatments**

**Table 1 Comparison of the available approaches to concomitant lithiasis of gallbladder and common bile duct**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Single-step** | **Advantages** | **Disadvantages** | **Risks** | **Availability** |
| Open cholecystectomy and bile duct clearance | Highly effective | Highly invasive | Surgical complications, Kehr positioning | All hospitals |
| Fully laparoscopic cholecystectomy and bile duct clearance | Very effective | Highly less invasive | Kehr positioning | Few hospitals |
| Laparoscopic cholecystectomy and intraoperative endoscopic bile duct clearance | Very effective | Less invasive | Endoscopic complications | Few hospitals |
| **Two-step** |  |  |  |  |
| Preoperative endoscopic bile duct clearance and sequential laparoscopic cholecystectomy | Very effective | Less invasive | Unnecessary ERCP, Endoscopic complications | Most hospitals |
| Laparoscopic cholecystectomy and sequential endoscopic bile duct clearance | Effective | Less invasive | Endoscopic complications, Further procedures | Most hospitals |

ERCP: Endoscopic retrograde cholangiography.