

Common bile duct stones management: A network meta-analysis

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BACKGROUND:	Timely management is critical for treating symptomatic common bile duct (CBD) stones; however, a single optimal management strategy has yet to be defined in the acute care setting. Consequently, this systematic review and network meta-analysis, comparing one-stage (CBD exploration or intraoperative endoscopic retrograde cholangiopancreatography [ERCP] with simultaneous cholecystectomy) and two-stage (precholecystectomy or postcholecystectomy ERCP) procedures, was undertaken with the main outcomes of interest being postprocedural complications and hospital length of stay (LOS).
METHODS:	PubMed, SCOPUS, MEDLINE, Embase, and Cochrane Central Register of Controlled Trials were methodically queried for articles from 2010 to 2021. The search terms were a combination of medical subject headings terms and the subsequent terms: gallstone; common bile duct (stone); choledocholithiasis; cholecystitis; endoscopic retrograde cholangiography/ERCP; common bile duct exploration; intraoperative, preoperative, perioperative, and postoperative endoscopic retrograde cholangiography; stone extraction; and one-stage and two-stage procedure. Studies that compared two procedures or more were included, whereas studies not recording complications (bile leak, hemorrhage, pancreatitis, perforation, intra-abdominal infections, and other infections) or LOS were excluded. A network meta-analysis was conducted to compare the four different approaches for managing CBD stones.
RESULTS:	A total of 16 studies (8,644 participants) addressing the LOS and 41 studies (19,756 participants) addressing postprocedural complications were included in the analysis. The one-stage approaches were associated with a decrease in LOS compared with the two-stage approaches. Common bile duct exploration demonstrated a lower overall risk of complications compared with preoperative ERCP, but there were no differences in the overall risk of complications in the remaining comparisons. However, differences in <i>specific</i> postprocedural complications were detected between the four different approaches managing CBD stones.
CONCLUSION:	This network meta-analysis suggests that both laparoscopic CBD exploration and intraoperative ERCP have equally good outcomes and provide a preferable single-anesthesia patient pathway with a shorter overall length of hospital stay compared with the two-stage approaches. (<i>J Trauma Acute Care Surg.</i> 2022;93: e155–e165. Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.)
LEVEL OF EVIDENCE:	Systematic Review/Meta Analysis; Level III.
KEY WORDS:	Common bile duct stone; choledocholithiasis; ERCP; common bile duct exploration; one- and two-stage procedure.

Common bile duct (CBD) stones are frequently encountered in the surgical practice of acute care surgeons. Up to 20% of patients requiring urgent cholecystectomy for acute cholecystitis have been found to have concomitant CBD stones.^{1–3} Despite being a common surgical condition, the optimal management of CBD stones in the acute setting has been highly debated. In the last several decades, the surgical approach for treating complicated biliary calculous diseases has fundamentally changed from open to laparoscopic.^{4,5} With the introduction of endoscopic retrograde cholangiopancreatography (ERCP) in 1968, the interventional approach to CBD stones shifted in favor of a two-stage approach, either precholecystectomy (preERCP) or postcholecystectomy (postERCP).^{4,5} More recently, the one-stage approach with intraoperative ERCP (iERCP) or laparoscopic CBD exploration (CBDE) by choledochoscopy and cholecystectomy has become a strong contender to the one-stage open surgical CBDE, that is, choledochotomy plus cholecystectomy.^{6,7}

Since acute care surgeons commonly manage CBD stone-related conditions, it is important to establish evidence-based best practice for this patient population to improve resource allocation and training, decrease disease- and procedural-specific complications, and improve overall patient throughput in the hos-

pital. Moreover, it is important to understand the application and associated outcomes of multiple different approaches to a complicated disease process such as choledocholithiasis, so therapy can also be tailored to an individual center, surgeon, or patient.

To this end, we undertook a systematic review and network meta-analysis comparing the different treatment options for CBD stones. The main outcomes of interest were postoperative complications and hospital length of stay (LOS), when comparing the one-stage and two-stage approaches.

PATIENTS AND METHODS

Eligibility Criteria

This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Supplementary Table 1, <http://links.lww.com/TA/C649>).⁸ No protocol was used for the systemic review. We included studies that met the following inclusion criteria: (a) the study design was either an observational cohort study, case-control, or randomized control trial investigating the management of choledocholithiasis; (b) patients were managed using CBDE, iERCP, preERCP, or postERCP; (c) the

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experimental group(s) and the control group received different treatments; and (d) the study recorded complications and/or LOS in all groups. Studies were excluded based on the following criteria: (a) irrelevant studies; (b) duplicate studies; (c) unavailable data in the manuscript; (d) studies unavailable in English or English translation; (e) studies for which a full text was unavailable; (f) studies not indexed by MEDLINE; (g) previous systematic reviews and meta-analyses as well as reviews, letters, and case reports; and (h) the mean LOS was reported without an SD or the median LOS was reported without an interquartile range (IQR).

Search Methodology

PubMed, SCOPUS, MEDLINE, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL) were methodically searched from January 2010 to December 2021. The initial search was from 2000; however, since many of the studies included patients from the end of 1900s or very early in the 2000s, the decision was made to concentrate on the studies published from 2010 and beyond. The search terms were a combination of medical subject headings terms and the subsequent terms: gallstone; common bile duct (stone); choledocholithiasis; cholecystitis; endoscopic retrograde cholangiography/ERCP; common bile duct exploration; intraoperative, preoperative, perioperative, and postoperative endoscopic retrograde cholangiography; stone extraction; and one-stage and two-stage procedure.

Study Selection

Using the web-based software platform Covidence, several investigators screened the original studies independently based on the previously mentioned inclusion and exclusion criteria. An initial review was performed of the article abstracts and titles, after which each reviewer would cast a vote using the software platform to include or exclude the study from further review. Votes from two independent investigators were required to include or exclude a study. Investigators performed a full-text review of the remaining articles after the initial screening. Studies that received votes for inclusion from two independent investigators were retained for the final analysis. Any discrepancies in voting were addressed by discussion or third-party consensus.

Data Extraction

All data were extracted from eligible studies using a standardized protocol. The following information was retrieved: PubMed unique identifier, authors' names, publication year, the country where the study was conducted, study design, study subjects, the number of participants, the number of male and female participants, the range of years covered by the study, case and control procedure, the number of patients who underwent the case and control procedure, the number of patients lost to further analysis, the number of patients with and without any complication for the case and control procedures, the number of patients with and without a specific complication for the case and control procedures (these included bile leak, hemorrhage, pancreatitis, perforation, intra-abdominal infections, and other infections), and mean and SD or median and IQR for LOS.

Quality Assessment

The risk of bias was evaluated in conjunction with the data extraction using the Cochrane Suggested Risk of Bias criteria for Ef-

fective Practice and Organization of Care reviews: random sequence generation, allocation concealment, baseline outcome measurements similar, baseline characteristics similar, incomplete outcome data, knowledge of the allocated interventions adequately prevented during the study, protection against contamination, selective outcome reporting, and other risks of bias. A quality score was calculated for each study as the sum of the number of criteria that were classified as low risk. If a criterion could not be definitively classified as high or low risk, it was counted as half a point instead.

Outcomes

The primary outcomes of interest were the overall risk of complications and the total hospital LOS. The secondary outcomes of interest were the risk of bile leak, hemorrhage, pancreatitis, perforation, intra-abdominal infections, and other infections.

Statistical Analysis

The mean difference (MD) for LOS and corresponding standard error of MD were calculated using the following formulae:

$$MD = \text{mean}_1 - \text{mean}_2$$

$$SE_{MD} = \sqrt{\left(\frac{N_1 s_1^2 + N_2 s_2^2}{N_1 + N_2 - 2}\right) \left(\frac{N_1 + N_2}{N_1 N_2}\right)}$$

where mean, s , and N correspond to the mean LOS, SD of LOS, and number of patients, respectively. According to the Cochrane Handbook, if the median and IQR were provided instead of the mean and SD, the mean and SD were estimated using the median and IQR.⁹ An MD <0 indicates that treatment 1 has a shorter mean LOS than treatment 2. If the 95% confidence interval (CI) for the MD contains 0, there is no statistically significant difference between the treatment groups.

The risk ratio (RR) and corresponding standard error of the natural log-transformed RR (log(RR)) were calculated using the extracted numbers according to the formulae below for all complications and specific complications:

$$RR = \frac{n_1/N_1}{n_2/N_2}$$

$$SE_{\log(RR)} = \sqrt{\frac{N_1 - n_1}{N_1 n_1} + \frac{N_2 - n_2}{N_2 n_2}}$$

where n_1 is the number of patients with complications in treatment group 1, N_1 is the total number of patients in treatment group 1, n_2 is the number of patients with complications in treatment group 2, and N_2 is the total number of patients in treatment group 2. According to the Cochrane Handbook, if n_1 or n_2 was 0, it was replaced by 0.5.⁹ An RR <1 indicates that treatment 1 had a lower risk for complication(s) than treatment 2. If the 95% CI for the RR contains 1, there is no statistically significant difference between the treatment groups.

The direct effect for every potential pair of treatments was evaluated using conventional meta-analyses. The Q test and I^2 index were used to evaluate the heterogeneity of each effect size. An I^2 index <50% indicates that the studies have good homogeneity, and the fixed-effects model was used; otherwise, a random-

effects model was used. If an indirect effect between two treatments existed, it was derived using the method described by Dias et al.¹⁰ Subsequently, a network meta-analysis was used to combine both the direct and indirect effects for comparison.¹⁰

The net splitting method was used to diagnose inconsistency between the direct and indirect effects.¹¹ The direct, indirect, and combined effects were presented using forest plots. The comparison-adjusted funnel plots were used to visualize the risk of publication bias in the network meta-analyses; the numerical Egger's test for publication bias was also used where possible.¹² A ranking probability plot was used to rank the treatments (a high value indicates that the treatment might be better). The rank probability was calculated according to the method suggested by Rücker et al.¹³

The statistical analyses were completed in R 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria) using packages meta, metafor, and netmeta.^{11,14,15}

RESULTS

Study Selection Outcome and Characteristics

The search identified 1,920 potential articles for inclusion, after excluding duplicates. A total of 348 studies remained after the initial review of titles and abstracts. Finally, 16 studies ($n = 8,644$) addressing the LOS and 41 studies ($n = 19,756$) addressing postprocedural complications were retained for the analysis (Supplementary Figs. 1 and 2, <http://links.lww.com/TA/C650>). The average ages of the participants included in these studies were 54.2 and 54.1 years for the LOS and postprocedural complications studies, respectively.

Study Quality Assessment

The quality of the included studies varied in terms of quality score (the total score is 10 with 10 reflecting the highest quality study) from 2.5 to 7.5, with a median score of 5.5.

Laparoscopic CBDE Compared With Precholecystectomy or Postcholecystectomy ERCP

According to the rank probabilities, for overall complications and specific complications including bleeding, pancreatitis, and perforation, CBDE was better than preERCP and postERCP (Fig. 1). Regarding LOS, although the point estimate for CBDE indicated a longer LOS than postERCP, the difference was not statistically significant (MD, 0.36; 95% CI, -1.26 to 1.98; Fig. 2). However, there was a significantly reduced LOS in the CBDE cohort compared with the preERCP cohort (MD, -2.02; 95% CI, -3.04 to -1.01; Fig. 2). The relative risk of all complications was also reduced in the CBDE cohort compared with the preERCP group (RR, 0.77; 95% CI, 0.59–0.99; Fig. 3), whereas no difference was observed compared with the postERCP group. The risk of bile leak was three times higher in the CBDE group compared with preERCP (RR, 3.31; 95% CI, 2.00–5.46; Fig. 4), while no difference was found when comparing CBDE to postERCP (RR, 1.37; 95% CI, 0.68–2.78; Fig. 4). The risk of pancreatitis was reduced by almost 80% in the CBDE group compared with both preERCP (RR, 0.22; 95% CI, 0.12–0.40; Fig. 5) and postERCP (RR, 0.24; 95% CI, 0.13–0.46; Fig. 5). No difference was detected in the risk of iatrogenic perforation (Fig. 6), hemorrhage (Supplementary Fig. 3, <http://links.lww.com/TA/C650>), intra-abdominal infections (Supplementary Fig. 4, <http://links.lww.com/TA/C650>), or other infections (Supplementary Fig. 5, <http://links.lww.com/TA/C650>) when comparing CBDE and iERCP.

com/TA/C650), intra-abdominal infections (Supplementary Fig. 4, <http://links.lww.com/TA/C650>), or other infections (Supplementary Fig. 5, <http://links.lww.com/TA/C650>) between preERCP or postERCP and CBDE.

iERCP Compared With Precholecystectomy and Postcholecystectomy ERCP

Regarding LOS and the overall risk of complications, iERCP was superior to both preERCP and postERCP according to the rank probabilities (Fig. 1). According to the rank probabilities, iERCP was also better than preERCP or postERCP for intra-abdominal infections (Fig. 1). The network meta-analysis demonstrated a significantly reduced LOS in the iERCP cohort compared with the preERCP cohort (MD, -3.12; 95% CI, -3.91 to -2.32; Fig. 2) but no statistical difference compared with postERCP group (Fig. 2). Although the point estimates for the iERCP cohort indicated a lower overall risk of complications compared with preERCP and postERCP, the results were not statistically significant (Fig. 3). The risk of bile leak was almost halved in the iERCP cohort compared with the postERCP group (RR, 0.56; 95% CI, 0.37–0.84; Fig. 4); however, no statistically significant difference was detected when iERCP was compared with the preERCP (RR, 1.35; 95% CI, 0.80–2.27; Fig. 4). The risk of intra-abdominal infections was lower after iERCP compared with postERCP (RR, 0.65; 95% CI, 0.44–0.94; Supplementary Fig. 4, <http://links.lww.com/TA/C650>). There was no statistically significant difference detected in the risk of pancreatitis (Fig. 5), iatrogenic perforation (Fig. 6), hemorrhage (Supplementary Fig. 3, <http://links.lww.com/TA/C650>), or other infections (Supplementary Fig. 5, <http://links.lww.com/TA/C650>) when comparing iERCP with preERCP and postERCP cohorts.

Laparoscopic CBDE Compared With iERCP

iERCP demonstrated a higher probability of being better than CBDE in terms of LOS (Fig. 1), with a significantly lower LOS than CBDE (MD, -1.09; 95% CI, -2.15 to -0.04; Fig. 2). Regarding the overall risk of complications, CBDE was better than iERCP based on the rank probabilities (Fig. 1). However, the difference was not statistically significant (RR, 0.94; 95% CI, 0.70–1.26; Fig. 3). For specific complications, CBDE was superior to iERCP regarding the risk of hemorrhage, pancreatitis, and perforation (Fig. 1). Common bile duct exploration was associated with twice the risk of bile leak compared with iERCP (RR, 2.45; 95% CI, 1.33–4.52; Fig. 4). The relative risk of pancreatitis was reduced by 78% in the CBDE cohort compared with the iERCP cohort (RR, 0.22; 95% CI, 0.12–0.41; Fig. 5). The risk of iatrogenic perforation was reduced by 86% in patients who underwent CBDE (RR, 0.14; 95% CI, 0.02–0.93; Fig. 6); however, this was only based on the indirect comparison. There was no statistically significant difference detected in the risk of hemorrhage (Supplementary Fig. 3, <http://links.lww.com/TA/C650>), intra-abdominal infections (Supplementary Fig. 4, <http://links.lww.com/TA/C650>), or other infections (Supplementary Fig. 5, <http://links.lww.com/TA/C650>), when comparing CBDE and iERCP.

Publication Bias

Funnel plots of all the studies included as a part of the network meta-analysis were created to graphically determine

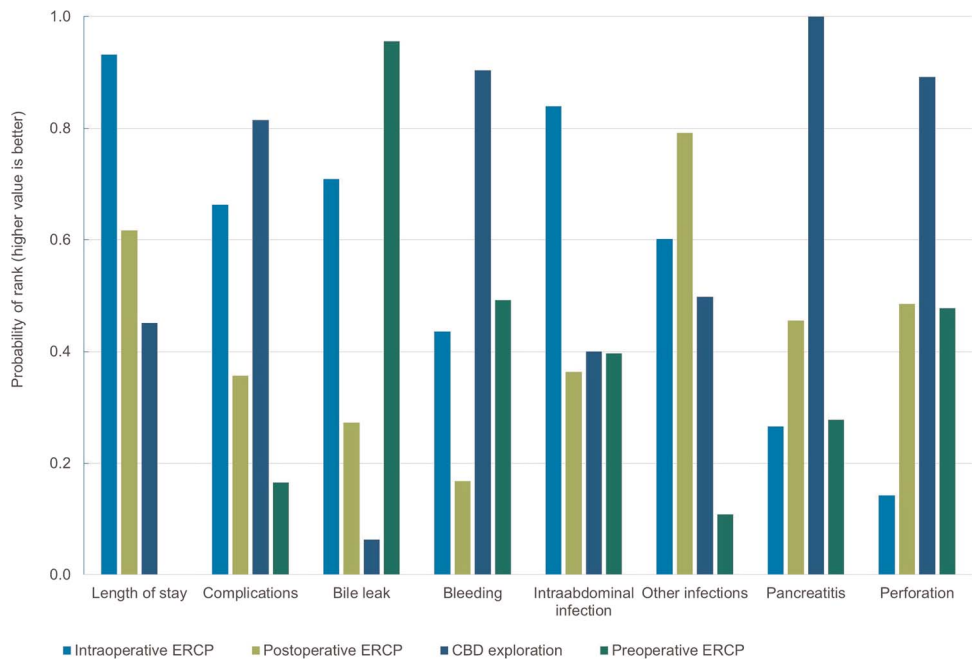


Figure 1. Ranking of procedures. *Because of the low value calculated for preoperative ERCP in regard to LOS, this bar is not visible in the figure.

the presence of publication bias (Supplementary Figs. 6–13, <http://links.lww.com/TA/C650>). In general, studies were distributed within or close to the 95% CI for all outcomes, which indicated a homogenous distribution of the study results. The nonsignificant *p* values derived from Egger's test further support this conclusion. Collectively, these results indicate no statistically significant publication bias in the in-

cluded articles that would impact the meta-analysis estimates of effect size.

DISCUSSION

There is consensus that timely management is critical for treating CBD stones, particularly those that are symptomatic,

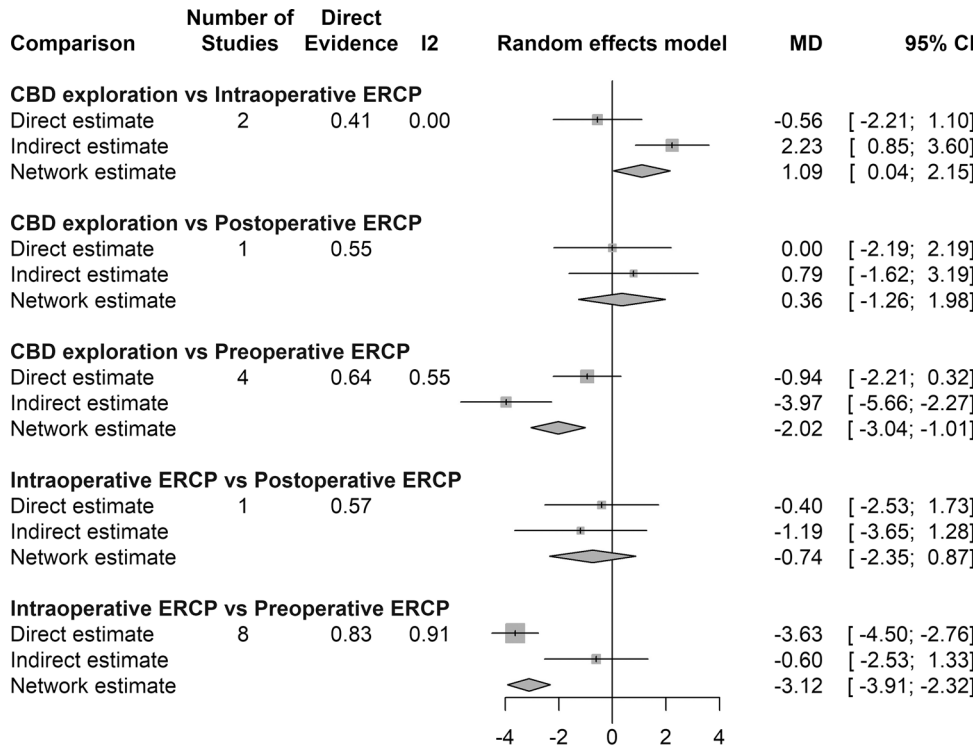


Figure 2. Network meta-analysis of hospital LOS.

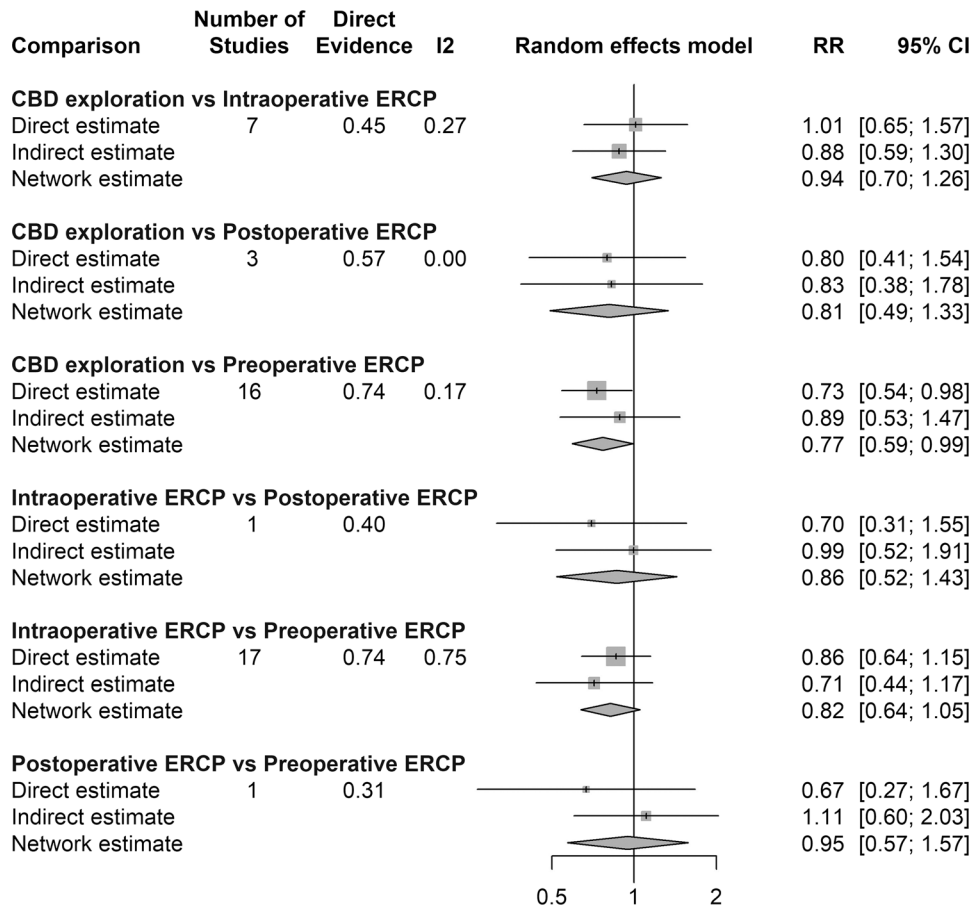


Figure 3. Network meta-analysis of the overall risk of complications.

while improving patient throughput in the hospital. However, a single optimal management strategy has yet to be defined in the acute care setting.

Watchful Waiting

It is important to recognize that even asymptomatic CBD stones confer a high risk of complications. In a cohort of patients with incidental CBD stones diagnosed by imaging in asymptomatic patients, biliary complications developed in 6.1% of patients after 1 year, 11% after 3 years, and 17% after 5 years.¹⁶ Unfavorable outcomes have also been reported in 16% to 36% of patients when no intervention was undertaken for CBD stones diagnosed by intraoperative cholangiogram, depending on the size of the calculi.¹⁷ These results are in line with a recent population-based registry study from Sweden conducted by Johansson et al.¹⁸ comparing surveillance to intervention for CBD stones found on intraoperative cholangiogram. They reported a fivefold increase in the risk of needing to perform an unplanned postERCP because of retained stone(s) in the surveillance group compared with the intervention group (adjusted HR, 5.5 [95% CI, 4.8–6.4]; $p < 0.005$). For smaller stones (<4 mm in diameter), the risk of an unplanned postERCP was three times higher in the surveillance group (adjusted HR, 3.5 [95% CI, 2.4–5.1]; $p < 0.005$).¹⁸ However, there is still an ongoing debate about the ideal approach and value to a “wait-and-see” approach for entirely asymptomatic CBD stones that are discovered only on imaging or by intraoperative cholangi-

ography, where multiple series have demonstrated that the majority of these stones will pass spontaneously and will not require further intervention or hospitalization.^{1,19,20} Nevertheless, most patients with CBD calculi admitted to acute care surgical services present with one or more symptoms and conditions related to the presence of CBD stone(s), such as abdominal pain, jaundice, cholecystitis, cholangitis, and pancreatitis, which necessitates an active rather than a “wait-and-see” approach.

ERCP Without Cholecystectomy

Cholecystectomy after ERCP for CBD stones has been widely debated, especially in the elderly.²¹ Deferring postERCP cholecystectomy has been associated with higher rates of morbidity and readmissions.^{22–24} More than 25% of cases eventually require a cholecystectomy.^{21,24} In a meta-analysis that included 1,605 patients, 864 (53.8%) had their cholecystectomy deferred following ERCP with sphincterotomy, of whom 26% required a cholecystectomy.²⁴ Furthermore, a total of 37% of patients with in situ gallbladders suffered a complication from remaining stones. Compared with a prophylactic cholecystectomy, deferred cholecystectomy resulted in a significantly increased risk of mortality (odds ratio [OR], 2.56 [95% CI, 1.54–4.23]; $p < 0.0001$). Patients who did not undergo a prophylactic cholecystectomy were also more likely to develop recurrent biliary pain and cholecystitis (OR, 5.10 [95% CI, 3.39–7.67]; $p < 0.0001$). However, the rate of pancreatitis (OR, 3.11 [95%

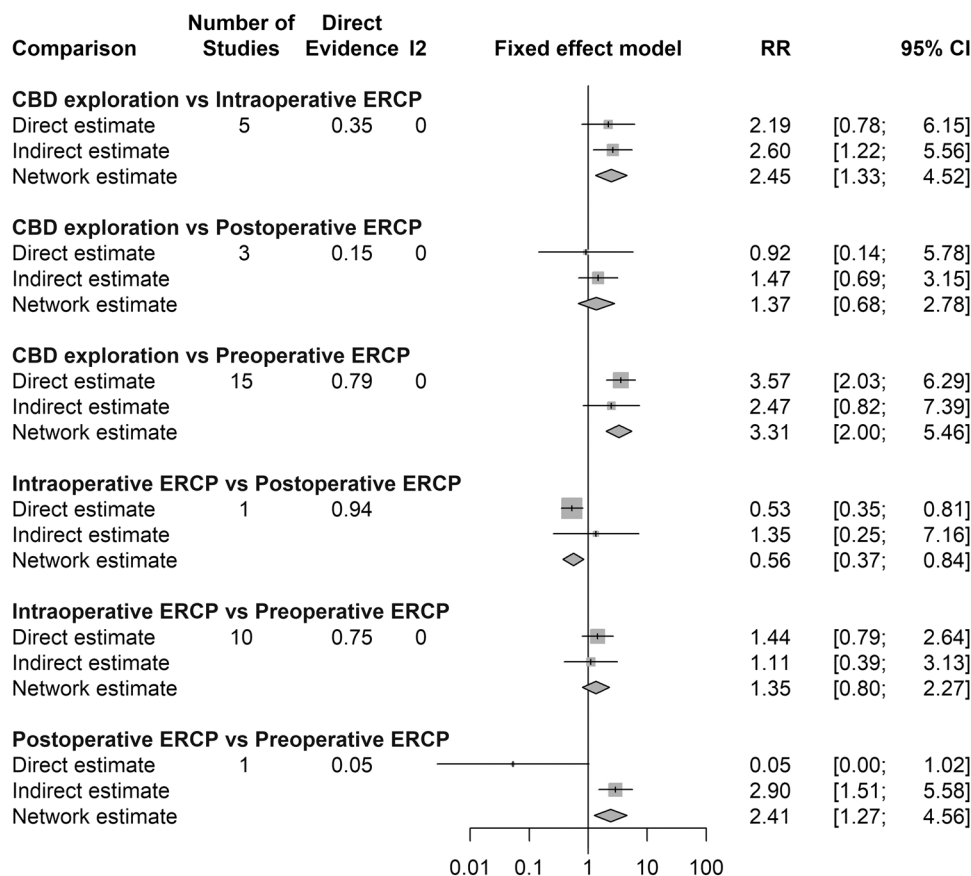


Figure 4. Network meta-analysis of the risk of postprocedure bile leak.

CI, 0.99–9.83]; $p = 0.053$) and cholangitis (OR, 1.49 [95% CI, 0.74–2.98]; $p = 0.264$) was unaffected.²⁴ These findings favor performing postERCP cholecystectomy, preferably during the index admission rather than as a postponed elective operation.

In practice, most patients deferred from an index admission cholecystectomy are older, burdened by comorbidities, and frail, which makes managing CBD stone-related complications even more challenging.^{21,23–25} With a growing elderly patient population worldwide, gallstone-related diseases and interventions will also increase; this includes cholecystectomy for acute cholecystitis, which has a threefold higher risk of CBD stones than elective cholecystectomy.^{26,27} Currently, guidelines do not make a distinction in the optimal timing of acute cholecystectomy for cholecystitis when comparing elderly and younger patients. Instead, surgery during the index admission is recommended for all ages, where no absolute contraindication to surgery exists.^{28,29} Even in octogenarians, postERCP laparoscopic cholecystectomy has been shown to be safe.³⁰ Nevertheless, the risks associated with a more technically challenging operation postERCP should not be underestimated, and decision about surgery versus observation should be tailored to the patient and the individual risk-benefit analysis.³¹

Laparoscopic CBDE Versus Precholecystectomy or Postcholecystectomy ERCP

The use of laparoscopic CBDE has been steadily declining in the United States in favor of the two-stage approach using

ERCP and cholecystectomy.⁵ Despite both approaches exhibiting comparable safety and efficacy, the one-stage CBDE strategy seems superior in terms of shorter LOS, need for fewer procedures, and cost-effectiveness.^{1,32,33} The current analyses found a lower overall risk of complications and a reduced LOS in patients undergoing CBDE compared with preERCP; however, CBDE and postERCP did not differ significantly. When comparing specific complications, CBDE had an 80% lower risk of pancreatitis than preERCP and postERCP, whereas no differences were observed in the risk of hemorrhage, perforation, or infectious complications. The risk of bile leak was three times higher in CBDE patients compared with preERCP; nonetheless, this difference was not present when comparing CBDE to postERCP. The overall LOS was on average 2 days shorter in patients undergoing CBDE compared with preERCP. This is likely due to the logistical challenges of scheduling an ERCP, which is usually performed by gastroenterologists rather than surgeons. In summary, these results support a one-stage CBDE approach over the two-stage approaches.

iERCP Versus Precholecystectomy or Postcholecystectomy ERCP

A Cochrane review from 2018 that included 5 randomized trials with a total of 517 patients (257 patients who underwent a rendezvous ERCP and cholecystectomy and 260 patients who underwent a two-stage approach) concluded that there was no difference between iERCP and preERCP in regard to the overall

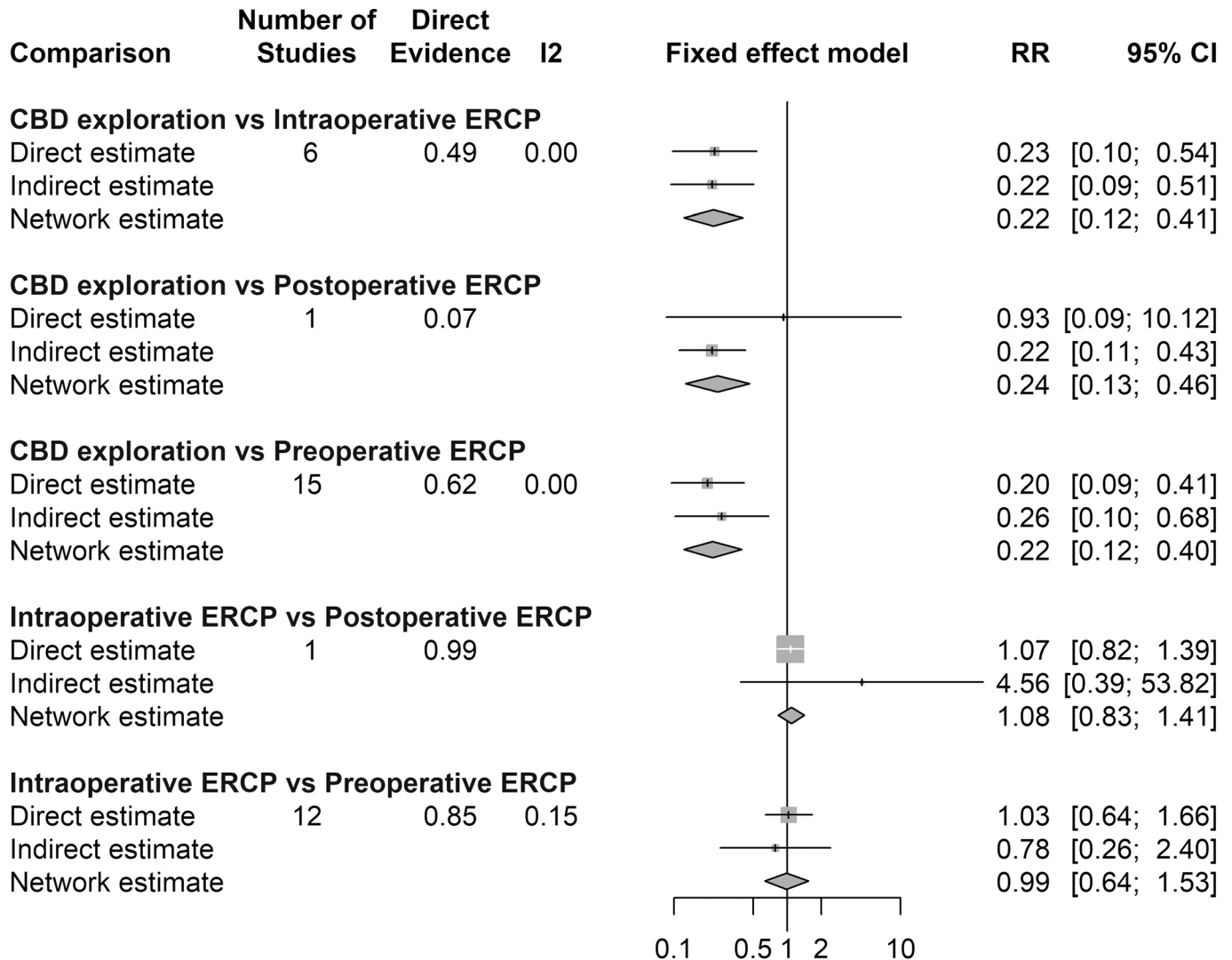


Figure 5. Network meta-analysis of the risk of postprocedure pancreatitis.

morbidity and mortality rates.³⁴ This is in line with recent studies comparing the two different approaches²³ and mirrors the result of the current study. Pancreatitis, a feared complication resulting from accidentally cannulating the pancreatic duct or the increased pressure caused by the contrast injection, occurs in up to 7% of ERCP cases.^{35,36} However, the use of the rendezvous technique during iERCP is increasing,⁶ which may mitigate this risk.³⁵ In a meta-analysis by Lin et al.³⁷ that included 1,061 patients, of whom 542 underwent a rendezvous iERCP and 519 underwent a postcholecystectomy ERCP, the authors reported a 74% decreased odds of postprocedural pancreatitis in patients managed using the rendezvous technique (OR, 0.26; 95% CI, 0.12–0.54). They also reported a decrease in overall morbidity (OR, 0.41; 95% CI, 0.27–0.62) and LOS (MD [days], –3.52; 95% CI, –4.69 to –2.35). Nevertheless, they did not identify any significant differences in bile leak or hemorrhage risk when comparing the two approaches.³⁷ Another meta-analysis undertaken by Arezzo et al.,³⁸ which includes four randomized studies comparing the rendezvous iERCP to a two-stage approach, found an almost 50% decrease in the overall odds of complica-

tions (OR, 0.56; 95% CI, 0.32–0.99; $p = 0.04$) with a decrease in the odds of clinical pancreatitis by more than 70% in the iERCP group (OR, 0.33; 95% CI, 0.12–0.91; $p = 0.03$). In the current study, we did not observe a difference in the risk of pancreatitis between the iERCP and preERCP or postERCP groups. This is likely explained by all types of iERCP being included, that is, those performed with and without the rendezvous technique. Conversely, there was a decrease in the LOS by 3 days in the iERCP group compared with the preERCP group. These results favor a one-stage iERCP approach over the two-stage procedures.

Laparoscopic CBDE Versus iERCP

Previous studies have found that the one-stage CBDE and iERCP procedures are effective in CBD clearance compared with preERCP or postERCP.³⁹ However, in a randomized clinical trial by Poh et al.,³³ the rate of retained stones was higher in patients managed using CBDE compared with iERCP (42% vs. 15%). In a network meta-analysis by Ricci et al.³⁹ investigating the safety-to-efficacy ratio, expressed as the ratio of morbidity to

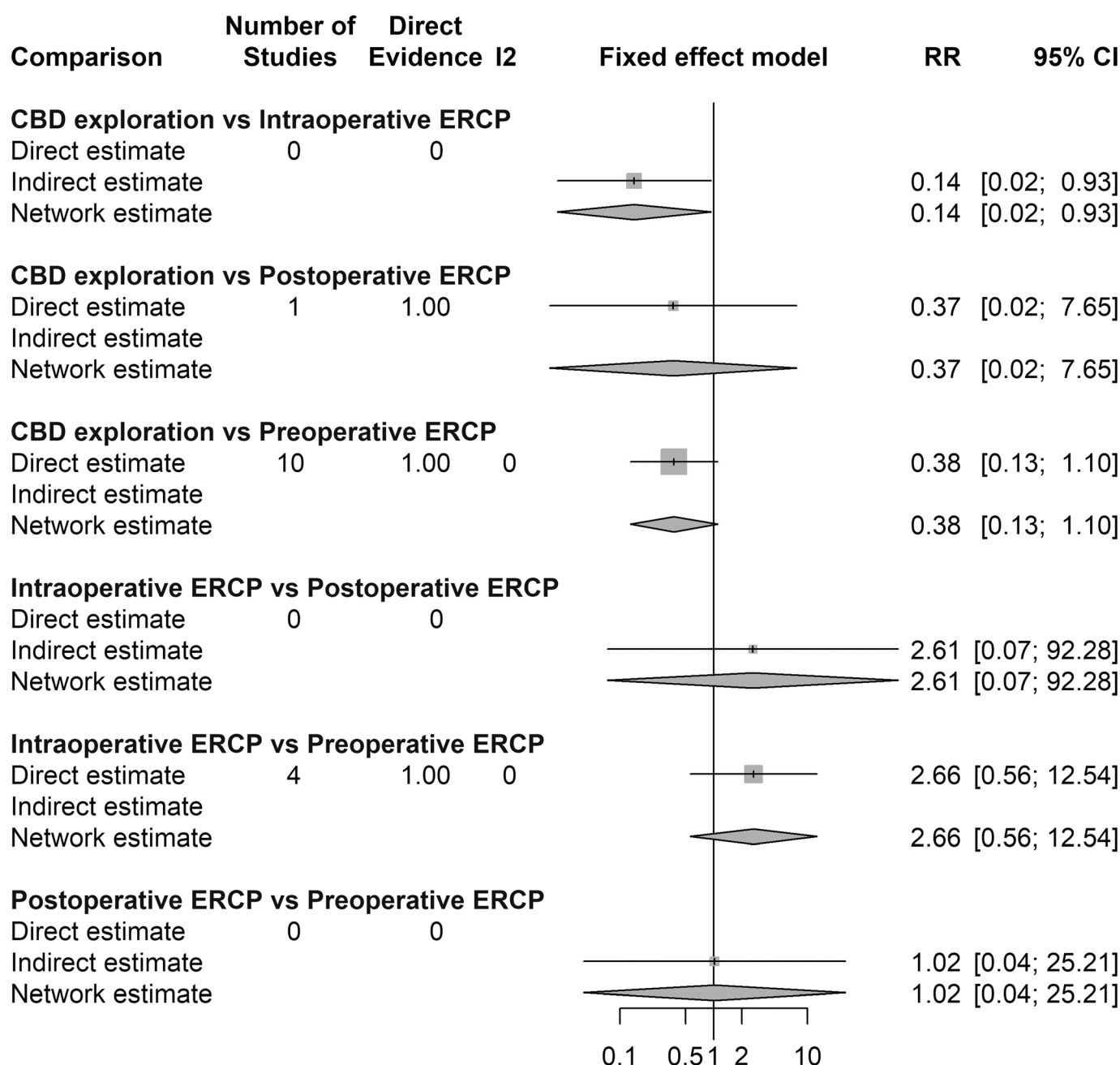


Figure 6. Network meta-analysis of the risk of perforation.

successful stone clearance, laparoscopic cholecystectomy with rendezvous iERCP was superior to the other three approaches. However, the network geometrics suggested that two main comparisons were lacking: postERCP versus iERCP and preERCP versus postERCP. Although the current network meta-analysis was unable to establish any differences in the overall rate of complications between CBDE and iERCP, there were significant differences in the risk of three specific complications: pancreatitis, perforation, and bile leak. Intraoperative ERCP was associated with a higher risk of pancreatitis and perforation. This is expected given the risk of cannulation of the pancreatic duct and sphincterotomy associated perforation when performing an ERCP. Conversely, the

risk of bile leak was significantly increased in patients who had undergone CBDE compared with iERCP. It is important to highlight that most biliary leaks necessitate additional interventions either with percutaneous drainage or CBD stenting, which is carried out through an ERCP. Granular data on the management of complications were not available in the studies included in the current investigation and were also out of the scope of the current paper.

Studies investigating the LOS either have reported results that favor iERCP or have been unable to find any differences compared with CBDE.^{33,40} The network meta-analysis in the current study indicated that iERCP was associated with a decrease in the total LOS by 1 day, on average, compared with CBDE.

CHALLENGES IN CLINICAL PRACTICE AND IMPLEMENTATION

Currently, hospitals and acute care services offer widely different approaches for managing CBD stones, largely based on the logistics involved, the managing physicians' skill sets, and individual provider preference. At most institutions, ERCP is performed by gastroenterologists, which necessitates the coordination of resources between different services, which can be time-consuming and incur the risk of delaying treatment. When resources are limited, such as during the COVID-19 pandemic, where most health care systems contended with a constant shortage of hospital beds, the one-stage approach would theoretically have been beneficial in reducing the time from admission to discharge, although this would also need to factor in the potentially increased average operative time required for either iERCP or CBDE. Although out of the scope of the current study, intuitively, the one-stage approaches could also reduce overall cost and increase patient satisfaction. The Acute Care Surgery subspecialty in Europe and the United States is still evolving; thus, additional exploration of different approaches to treating CBD stone disease is required to improve patient care.

LIMITATIONS

There are several limitations to be highlighted in the current study. There is a risk of selection bias since the included studies were required to have a comparison of ≥ 2 of the procedures. Studies describing only one procedure were excluded, as these descriptive studies lacked a comparison group, which is required for the meta-analysis. Furthermore, no distinction was made between choledocotomy or cholecystoscopy for CBDE, nor between iERCP performed using the rendezvous or traditional technique. Finally, the severity of complications was not available for further analysis. Nevertheless, to the authors' knowledge, this is the first study comparing common postprocedural complications and LOS across all four available interventions used for the management of CBD stones. The network meta-analysis allowed for a larger sample size, strengthening statistical power. Finally, a prospective randomized comparison of all four interventions for CBD stone management would be nearly impossible without introducing institutional biases or organizational and expertise limitations (Supplementary Data 1, <http://links.lww.com/TA/C651>).

CONCLUSION

Our network meta-analysis suggests that both laparoscopic CBDE and iERCP have equally good outcomes and may provide a preferable single-anesthesia patient pathway with a shorter overall length of hospital stay compared with the two-stage approaches.

AUTHORSHIP

S.M., G.A.B., B.S., and R.C. came up with the initial idea for the study. All authors have discussed and agreed before the start of the study on the study inclusion and exclusion criteria, analysis, and the main outcomes of interest. All authors have voted on the abstracts for further review. S.M., G.A.B., and M.P.F. reviewed manuscripts for inclusion in analysis. S.M., G.A.B., M.P.F., and Y.C. contributed in the data extraction and analysis. All authors contributed in the interpretation of data and results. S.M., G.A.B., M.P.F., Y.C., and R.C. contributed in drafting the manuscript. All

authors have critically reviewed and accepted the final version of manuscript submitted.

DISCLOSURE

The authors declare no conflicts of interest.

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