European Review for Medical and Pharmacological Sciences 2023; 27: 4656-4669

Comparison of laparoscopic common bile duct exploration and endoscopic retrograde cholangiopancreatography combined with laparoscopic cholecystectomy for patients with gallbladder and common bile duct stones a meta-analysis of randomized controlled trials

W.-F. LAN[1], J.-H. LI[2], Q.-B. WANG[1], X.-P. ZHAN[1], W.-L. YANG[1], L.-T. WANG[3], K.-Z. TANG[3]

[1]Department of Surgery, Suichang County People's Hospital, Lishui, China
[2]Department of Liver and Gall Surgery, Third Affiliated Hospital of Wenzhou Medical University, Wenzhou, China
[3]Department of Surgery, Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China

Weifeng Lan and Jinhai Li contributed equally to this study

Abstract. – OBJECTIVE: This study aimed to compare the efficacy and safety of laparoscopic common bile duct exploration (LCBDE) and endoscopic retrograde cholangiopancreatography (ERCP) combined with laparoscopic cholecystectomy (LC) to determine which one provides a better outcome for patients with gallbladder and common bile duct stones.

MATERIALS AND METHODS: An electronic literature search was undertaken using Embase, Medline, PubMed, and Cochrane Library databases up to April 2022. For quality assessment of included studies, randomized controlled trials (RCTs) were assessed by utilizing the Jadad scale. The primary outcome includes surgical success rate, retained stone rate, stone clearance rate, major morbidity, and mortality. The second outcome includes conversion to open surgery rate, postoperative pancreatitis, bile leakage, cholangitis, hemorrhage, pneumonia, and surgical-site infection.

RESULTS: 14 randomized controlled trials with 2,181 patients were included. No significant difference was seen between the two groups in terms of surgical success, stone clearance, retained stones, operation time, and total morbidity. LC-LCBDE had higher rate of bile leakage [relative risk (RR): 4.52; 95% confidence interval (CI): 2.19-9.31] and lower rate of postoperative pancreatitis (RR: 0.25; 95% CI: 0.13-0.46), cholangitis (RR: 0.17; 95% CI: 0.05-0.67), and hemorrhage (RR: 0.18; 95% CI: 0.07-0.42).

CONCLUSIONS: Both LC+LCBDE and LC+ERCP are safe, effective, and minimal-invasive treatments for concomitant gallbladder and CBD stones. LC-LCBDE was associated with comparable effects compared with LC+ERCP in terms of surgical success rate, stone clearance rate, retained stones rate, operation time, and total morbidity. At the same time, LC-LCBDE had a higher rate of bile leakage and a lower rate of postoperative pancreatitis, cholangitis, and hemorrhage.

Key Words:
Common bile duct stones, Laparoscopic common bile duct exploration, Endoscopic retrograde cholangiopancreatography, Laparoscopic cholecystectomy.

Introduction

Common bile duct stones (CBD) are detected in approximately 10-20% of patients with gallbladder stones and is associated with serious complications including acute obstruction suppurative cholangitis (AOSC) and pancreatitis[1,2]. The traditional open CBD exploration has been proven[2] as an effective treatment option. However, the severe invasive characteristics limited its application. As the development of new surgical techniques and concept of minimal invasive treatment, more and more alternatives have been explored for patients with CBD. The main minimal invasive approaches for concomitant gallbladder stones and CBD are laparoscopic cholecystectomy (LC)

Corresponding Author: Kezhong Tang, MD; e-mail: 2313055@zju.edu.cn

combined with laparoscopic common bile duct stones exploration (LCBDE) and LC combined endoscopic retrograde cholangiopancreatography (ERCP)[3,4]. According to the sequence of LC and ERCP, LC+ERCP treatments can be divided into three groups, preoperative ERCP followed by LC (ERCP/LC), intraoperative ERCP (LCERCP) and postoperative ERCP (LC/ERCP).

Compared with open cholecystectomy and CBD exploration, LC-LCBDE and LC+ERCP have their own advantage and have been recommended by many guidelines[5,6], including European Society of Gastrointestinal Endoscopy (ESGE) guideline[7]. The appropriate choice of LC-LCBDE and LC+ERCP is still controversial[7]. ERCP/LC is the preferred strategy for concomitant gallbladder stones and CBD stones in the world[8]. However, this two-step approach greatly increases the cost and length of hospital stay[9,10]. LCERCP seems to be a promising single-stage therapeutic regime with a better surgical success rate and shorter hospital stay, while this approach has some draw backs, such as higher rate of severe morbidity and mortality compared with LC-LCBDE[11]. After the first case of LCBDE reported by Petelin[12] in 1991, this approach is considered as a safe way to retain the function of the sphincter of Oddi and does not increase pressure of CBD during the treatment which result in lower rate of cholangitis and pancreatitis. However, LC-LCBDE also has its own disadvantages, such as higher rate of bile leakage, electrolyte disturbance and lower quality of life because of T-tube retaining, although the primary suture for CBD is more and more frequently recommended[13].

The surgical procedures and attributes of LC-LCBDE and LC+ERCP are different. Which one is better in terms of efficacy and safety has been controversial for a long time, with no current consensus[7]. Systematic review and meta-analysis are a possible solution to provide the best evidence based on the currently available studies. Shi et al[14] compared the efficacy and safety of LCBDE and ERCP based on 11 randomized controlled trials (RCTs) and concluded that both LC-LCBDE and LC+ERCP were highly effective in detecting and removing stones with similar rate of complications. However, they did not further analyze subgroups of LC+ERCP which had been described in detail. At the same time, it contained two studies[15,16] from the same institution and the same first author and based on the same database which should be excluded during analysis. Therefore, it is necessary to update and further verify the results. This meta-analysis included the latest and most comprehensive research to compare the efficacy and safety of LC-LCBDE and LC+ERCP to provide evidence for clinical application.

Materials and Methods

This study was performed according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines[17]. Ethical approval was not required in this study.

Literature Search Strategy

An electronic literature search was performed using Embase, Medline, PubMed, and Cochrane Library databases up to April 2022. Search terms included "common bile duct", "laparoscopic", "cholecystectomy" and "endoscopic". Two authors, Lan and Li, performed the electronic search independently in April 2022. Abstracts of the literatures were reviewed and collected according to the inclusion criteria. Any discordances for study inclusion between these 2 authors were settled in discussion with a third independent author. For quality assessment of included studies, RCTs were assessed by utilizing the Jadad scale[18].

Inclusion Criteria

All studies comparing LC-LCBDE and LC+ERCP had to meet the following criteria for inclusion: (1) compared LC-LCBDE with ERCP/LC or LCERCP or LC/ERCP in patients with gallbladder stones and confirmed or highly suspicious of CBD stones; (2) contained at least of one type of outcome interest in this study; (3) Only the most newly and completed studies were included in this study, when duplicated data were encountered; (4) study types were RCTs; (5) Articles published in English.

Exclusion Criteria

The exclusion criteria were as follows: (1) Single-arm study without a control group; (2) without original data to extract outcomes interest in this study; (3) without comparison of LC-LCBDE and LC+ERCP.

Outcome Measures for Meta-Analysis of Comparative Studies

The primary outcome measure evaluated was the relative risk (RR) for surgical success rate, retained stone rate, stone clearance rate, major morbidity, and mortality. The second outcome measure evaluated was RR for conversion to open surgery

rate, postoperative pancreatitis, bile leakage, cholangitis, hemorrhage, pneumonia, and surgical-site infection. Other information extracted from each study included author names, country, publication year, number of patients, study design and characteristics of patients enrolled. Any discrepancies in study eligibility or data extraction were reconciled.

Statistical Analysis

Two independent reviewers (L.W. and L.J.) extracted data from the collected articles by using a predefined data extraction form. RR and its variance were extracted from the study directly or required additional calculation from the data in the study. The simplest method consisted of the direct collection of RRs with 95% confidence interval (CI) described in the original study. Meta-analysis of the data was conducted using a random-effects model by Stata 12.0 (StataCorp, College Station, TX, USA). Inter-study heterogeneity was assessed using the χ^2 statistic and the I^2 value to measure the degree of variation not attributable to chance alone. This was graded as low (I^2<25%), moderate (I^2 25% to 75%) or high (I^2>75%). The significance level was set at p<0.05. Bias of publication was assessed by Egger and Begg tests.

Results

Search Results

Figure 1 showed the literature search flowchart. During the literature search we found 1,037 studies. After reviewing the titles and abstracts, 983 articles were excluded because they were review articles, editorials, nonhuman studies or non-English articles, not focusing on the review topic, and others not meeting the inclusion criteria. We identified 54 articles as potentially eligible for this review. However, 3 of these articles were case reports, 13 of them were without outcomes of related topic, 8 of them included patients without CBD stones, and 15 of them were single-arm studies.

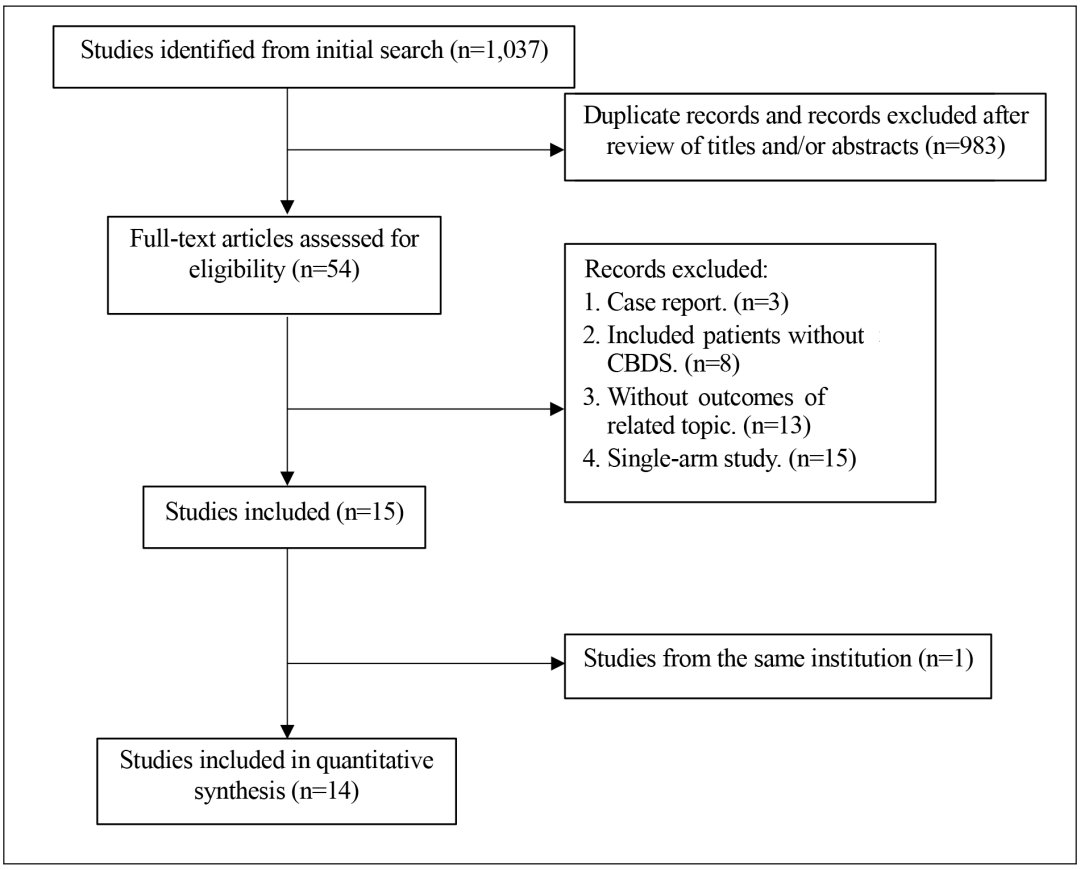

Figure 1. PRISMA flowchart describing literature search strategy.

15 eligible articles were selected. However, after careful evaluation, we found two studies reported by the same institution and authors based on the same database. We finally excluded one study published earlier with fewer information of patients. Finally, we included 14 studies[16,19-31] in this meta-analysis. In all these included 14 research articles were RCTs.

Characteristics of the Studies

In our meta-analysis, we included 14 RCTs[16,19-31] that evaluated the efficacy and safety of LC-LCBDE compared with LC+ERCP. In Table I, we reported the main characteristics of these studies. The total number of patients in the outcomes analysis of the included studies was 2,181 with median age of about 63 years. Four of the studies[21,29-31] were from China, two from UK and India[20,22,25,27], and one from USA[24], Italy[16], Egypt[23], Turkey[26], Cuba[19], and Australia[28] respectively. None of the studies included was from the same institution. Nine[16,19,22,24-27,29,31] of the studies researched about the comparison of LC-LCBDE and ERCP/LC, five[20,21,23,28,30] were about LC-LCBDE and LCERCP, and another one[25] was about LC-LCBDE and LC/ERCP. All RCTs included in the study obtained a score of more than three based on Jadad scale.

In Table II, a comprehensive comparison between LC-LCBDE and LC+ERCP was performed. The primary outcomes for these two kinds of approaches included operation time, surgical success rate, conversion to open operation rate, stone clearance rate, retained stone rate, hospital stay, and cost for operation. In Table III, a further comparison of morbidity and mortality between LC-LCBDE and LC+ERCP was performed. The secondary outcomes of this meta-analysis included postoperative pancreatitis, bile leakage, cholangitis, hemorrhage, pneumonia, and surgical-site infection.

Meta-Analysis of Primary Outcomes

Surgical success

Eleven[16,20-23,25-28,30,31] of fourteen studies reported data about the surgical success rate, and two[20,28] of them did not find any differences between these two approaches. Two studies[16,21] showed LC+ERCP could improve the rate of surgical success, while the other seven studies[22,23,25-27,30,31] found that LC-LCBDE was associated with an increased surgical success rate. The meta-analysis revealed that there was no difference in the surgical success rate between the two procedures both for every subgroup and the total (RR: 1.00; 95% CI: 0.94-1.07; Figure 2).

Retained stones

Ten[19-23,26-28,30,31] of fourteen studies reported data about the retained stones rate, and one[20] of them did not find any differences between these two approaches. Four studies[21,23,27,28] supported a higher retained stones rate in LC-LCBDE group. Poh et al[28] found the retained stones rate up to 42% in LC-LCBDE group compared with 15% in LCERCP group. The other five studies[19,22,26,30,31] found a lower retained stones rate in LC-LCBDE group. The meta-analysis revealed that there was no difference of surgical success rate between the two procedures (RR: 0.92; 95% CI: 0.45-1.88; Figure 3). For subgroup analysis, LC-LCBDE group obtained lower rate of retained stones compared with ERCP/LC group, though the result had no significant differences (RR: 0.46; 95% CI: 0.16-1.33; Figure 3).

Morbidity

The morbidity was reported in all studies[16,19-31]. Six[16,20,22,24,27,28] of fourteen studies supported a higher morbidity in LC-LCBDE group, while the other eight studies found a higher morbidity in LC+ERCP group. The meta-analysis revealed that LC-LCBDE group obtained lower rate of morbidity compared with LC+ERCP group, though the result had no significant differences (RR: 0.90; 95% CI: 0.69-1.17; Figure 4). A subgroup analysis also obtained the same results.

Stone clearance rate

Nine[16,19-23-26,28,29] of fourteen studies reported the data of CBD stone clearance rate, and two of them did not find any differences between these two approaches. The meta-analysis revealed that there was no difference of CBD stone clearance rate between the two procedures (RR: 1.00; 95% CI: 0.92-1.08; **Supplementary Figure 1**). For subgroup analysis, LC-LCBDE group obtained lower rate of CBD stone clearance rate compared with LCERCP group, though the result had no significant differences (RR: 0.91; 95% CI: 0.81-1.03; **Supplementary Figure 1**).

Mortality

Three[16,25,29] of fourteen studies reported the data of perioperative mortality rate. All the three studies indicated LC+ERCP group had higher rate of mortality compared with LC-LCBDE group.

Table I. The characteristics and quality assessment of the included studies.

Author	Year	Study period	Country	Design	Comparison	Cases	Age (year)	Sex (M/F)	Jadad score
Rhodes et al[20]	1998	1995-1997	UK	RCT	LCBDE	40	62 (24-83)	12/28	4
					LC/ERCP	40	68 (28-84)	14/26	
Cuschieri et al[16]	1999		Italy	RCT	LCBDE	150	19-88	60/90	4
					ERCP/LC	150	18-89	42/108	
Hong et al[21]	2006	2002-2003	China	RCT	LCBDE	141	48 (15-82)	28/65	3
					LCERCP	93			
Noble et al[22]	2009	2000-2006	UK	RCT	LCBDE	44	75.9 (70.0-80.8)	16/28	4
					ERCP/LC	47	74.3 (70.0-78.9)	22/25	
Rogers et al[24]	2010	1997-2003	USA	RCT	LCBDE	57			4
					ERCP/LC	55			
Bansal et al[25]	2010	2007-2008	India	RCT	LCBDE	15	47.1 (34-72)	4/11	4
					ERCP/LC	13	39.07 (23-64)	5/10	
ElGeidie et al[23]	2011	2009-2010	Egypt	RCT	LCBDE	115	32.5 (19-64)	29/86	4
					LCERCP	111	29.2 (20-67)	31/102	
Koc et al[26]	2013	2008-2010	Turkey	RCT	LCBDE	57	51.5 (23-69)	20/37	4
					ERCP/LC	54	54.9 (25-71)	18/36	
Bansal et al[27]	2014	2009-2012	India	RCT	LCBDE	84	45.1 (10-80)	23/61	3
					ERCP/LC	84	43 (17-80)	34/50	
Gonzalez et al[19]	2015	2007-2011	Cuba	RCT	LCBDE	100	56.3 (22-87)		3
					ERCP/LC	101	57.7 (20-84)		
					LCERCP	99	58.4 (23-87)		
Poh et al[28]	2016	2013-2015	Australia	RCT	LCBDE	52	53.4 (19.7)	23/29	4
					LCERCP	52	53.9 (22.6)	21/31	
Li et al[29]	2017	2014-2016	China	RCT	LCBDE	70	54.2±10.6	31/39	4
					ERCP/LC	70	53.2±11.3	33/37	
Liu et al[30]	2020	2010-2017	China	RCT	LCBDE	104	56.9 (19-78)	41/63	3
					LCERCP	103	57.1 (18-81)	42/61	
Zou et al[31]	2022	2018-2020	China	RCT	LCBDE	40	64.9±13.9	17/23	4
					ERCP/LC	40	67.8±13.4	19/21	

M male, F female, RCT randomized controlled trials, LCBDE laparoscopic common bile duct exploration, ERCP endoscopic retrograde cholangiopancreatography, LC laparoscopic cholecystectomy, ERCP/LC ERCP followed by LC, LCERCP LC with intraoperative ERCP, LC/ERCP LC followed by ERCP.

Table II. Summary of primary and secondary end points.

Author	Groups	Cases	Operative time (min)	Technical success (%)	Conversion to open surgery (%)	Stone clearance (%)	Retained stone rate (%)	Hospital stays (days)	Cost (USD)
Rhodes et al[20]	LCBDE	40	90 (25-310)	30 (75)	1 (2.5)	40 (100)	10 (25)	1 (1-26)	
	LC/ERCP	40	105 (60-255)	30 (75)	0	37 (92.5)	10 (25)	3.5 (1-11)	
Cuschieri et al[16]	LCBDE	150		90 (82.6)	19 (13)	126 (84)		6 (4.24-12)	
	ERCP/LC	150		129 (94.9)	7 (5)	126 (84)		9 (5.5-14)	
Hong et al[21]	LCBDE	141	133.83±58.24	126 (89.4)			3 (2.38)	4.66±3.07	2,128.6±541.9
	LCERCP	93	140.32±56.55	85 (91.4)			1 (1.17)	4.25±3.46	2,712.7±643.2
Noble et al[22]	LCBDE	44		44 (100)	4 (9.1)		0		
	ERCP/LC	47		45 (95.7)	2 (4.3)		1 (2.1)		
Rogers et al[24]	LCBDE	57				15 (88)		4 (1-17)	24,399 (11,190-60,138)
	ERCP/LC	55				30 (98)		5 (2-19)	26,656 (4,496-85,085)
Bansal et al[25]	LCBDE	15	153 (120-240)	14 (93.5)	1 (6.7)	15 (100)		4.2 (3-9)	
	ERCP/LC	13		9 (73.3)	2 (15.3)	11 (86.7)		4 (2-11)	
ElGeidie et al[23]	LCBDE	115	57 (45-145)	109 (94.8)	7 (6.1)	103 (92)	4 (3.6)	2.2 (1-9)	
	LCERCP	111	68 (45-160)	107 (96.4)	4 (3.6)	104 (97.2)	0.00%	3.1 (1-7)	
Koc et al[26]	LCBDE	57	93.47±32.06	55 (96.5)	0	55 (96.5)	2 (3.5)	3	
	ERCP/LC	54	113.33±36.07	51 (94.4)	1 (1.9)	51 (94.4)	3 (5.6)	6	
Bansal et al[27]	LCBDE	84	135.7 (80-240)	74 (88.1)	7 (8.3)		3 (3.6)	4.6 (2-15)	**3,3105.6**
	ERCP/LC	84	72.4 (30-150)	67 (79.8)	3 (3.6)		0	5.3 (2-37)	**4,2543.5**
Gonzalez et al[19]	LCBDE	100	117 (40-270)	0	42 (97.7)	2 (2.3)	2.1		
	ERCP/LC	101	98 (30-240)		0	42 (93.3)	11 (11.1)	3.1	
	LCERCP	99	94.2 (45-300)	0	45 (97.8)	2 (2.2)	1.2		
Poh et al[28]	LCBDE	52	110 (95-140)	48 (92.3)	0	36 (69)	22 (42)	3 (2-4)	
	LCERCP	52	112 (102-125)	48 (92)	3 (5.8)	45 (87)	8 (15)	2 (2-3)	
Li et al[29]	LCBDE	70	53.2±17.3		1 (1.43)	68 (97.14)		5.3±0.6	34,458±3,781
	ERCP/LC	70	57.5±15.1		7 (10)	60 (85.71)		5.1±0.7	54,188±4,006
Liu et al[30]	LCBDE	104	151±38	97 (93.3)	1 (1.0)		2 (1.9)	4 (2-9)	2,825.7±361.1
	LCERCP	103	171±46	85 (82.5)	6 (5.8)		8 (7.8)	6 (2-91)	4,552.6±643.6
Zou et al[31]	LCBDE	40	125.61±25.6	39 (97.5)			1 (2.5)	8.76±1.91	4,304.6±1,020.4
	ERCP/LC	40	79.52±28.1	38 (95)			3 (7.5)	9.59±3.78	5,898.0±948.2

Table III. Summary of morbidity and mortality of RCTs included in the study.

Author	Comparison	Total morbidity (%)	Perioperative mortality (%)	Pancreatitis (%)	Bile leakage (%)	Hemorrhage (%)	Cholangitis (%)	Pneumonia (%)	Surgical-site infection (%)
Rhodes et al[20]	LCBDE	7 (17.5)	0		3 (7.5)				
	LC/ERCP	6 (15)	0		1 (2.5)	4 (10)			
Cuschieri et al[16]	LCBDE	24 (15.8)	1 (0.75)	2 (1.5)				7 (4.7)	
	ERCP/LC	19 (12.8)	2 (1.5)	5 (3.3)		6 (4)		4 (2.7)	
Hong et al[21]	LCBDE	7 (5.55)		4 (2.8)	1 (0.71)			1 (0.71)	
	LCERCP	8 (9.41)		5 (5.4)	1 (1.1)			1 (1.1)	
Noble et al[22]	LCBDE	19 (43.2)							
	ERCP/LC	14 (29.8)							
Rogers et al[24]	LCBDE	6 (10.5)							
	ERCP/LC	5 (9.1)							
Bansal et al[25]	LCBDE	4 (26.7)			2 (13.3)				2 (13.3)
	ERCP/LC	4 (30.8)				1 (7.7)	1 (7.7)		2 (15.4)
ElGeidie et al[23]	LCBDE	8 (7.1)	0	1 (0.87)	5 (4.3)	1 (0.87)			2 (1.7)
	LCERCP	10 (9.3)	0	4 (3.6)	1 (0.9)	4 (3.6)			1 (0.9)
Koc et al[26]	LCBDE	2 (3.5)			2 (3.5)				
	ERCP/LC	3 (5.6)		2 (3.7)					
Bansal et al[27]	LCBDE	20 (23.8)			14 (16.7)				
	ERCP/LC	19 (22.6)	3 (3.6)	3 (3.6)	2 (2.4)	3 (3.6)	1 (1.2)		
Gonzalez et al[19]	LCBDE	2 (4.7)	0		2 (4.7)				
	ERCP/LC	6 (13.3)	0	2 (4.4)			4 (8.8)		
	LCERCP	0	0						
Poh et al[28]	LCBDE	20 (38)		2 (4)	2 (4)	1 (2)		2 (4)	2 (4)
	LCERCP	14 (27)		4 (8)	0	4 (8)			
Li et al[29]	LCBDE	2 (2.86)	0		1 (1.43)				
	ERCP/LC	10 (14.29)	1 (1.43)	6 (8.6)		1 (1.43)	2 (2.86)		
Liu et al[30]	LCBDE	19 (18)		2 (1.9)	2 (1.9)				
	LCERCP	31 (30)		21 (20.4)		4 (3.9)	5 (4.9)		
Zou et al[31]	LCBDE	6 (15)		0	5 (12.5)	1 (2.5)			
	ERCP/LC	13 (32.5)		7 (17.5)	0	6 (15)			

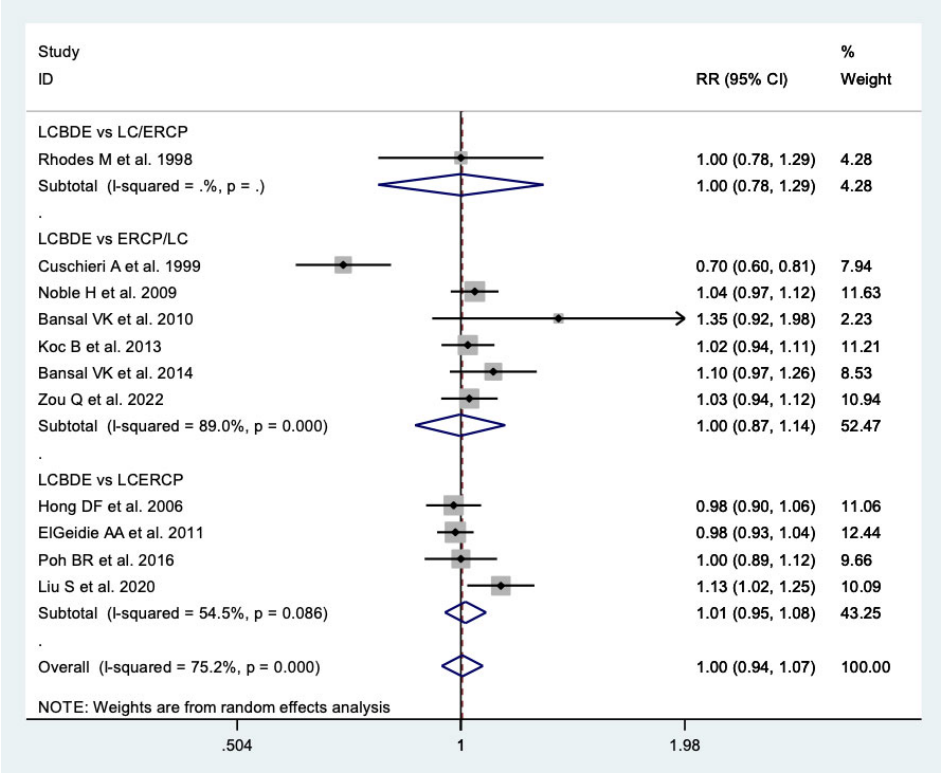

Figure 2. Forest plot for surgical success between LCBDE and LC+ERCP for treating gallstones with CBD stones.

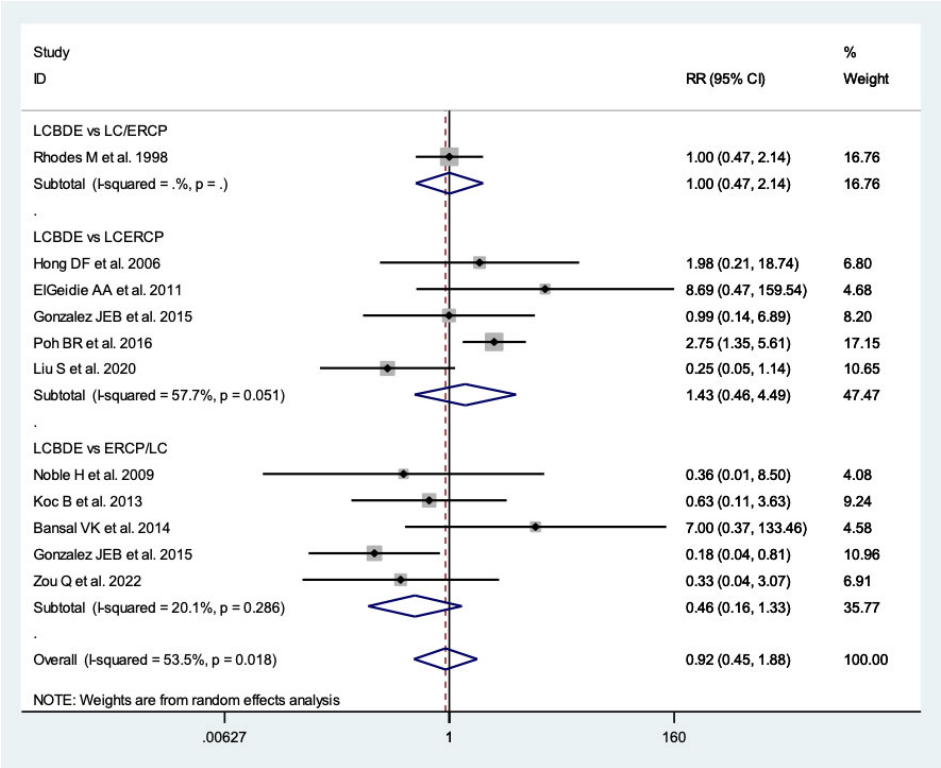

Figure 3. Forest plot for retained stone between LCBDE and LC+ERCP for treating gallstones with CBD stones.

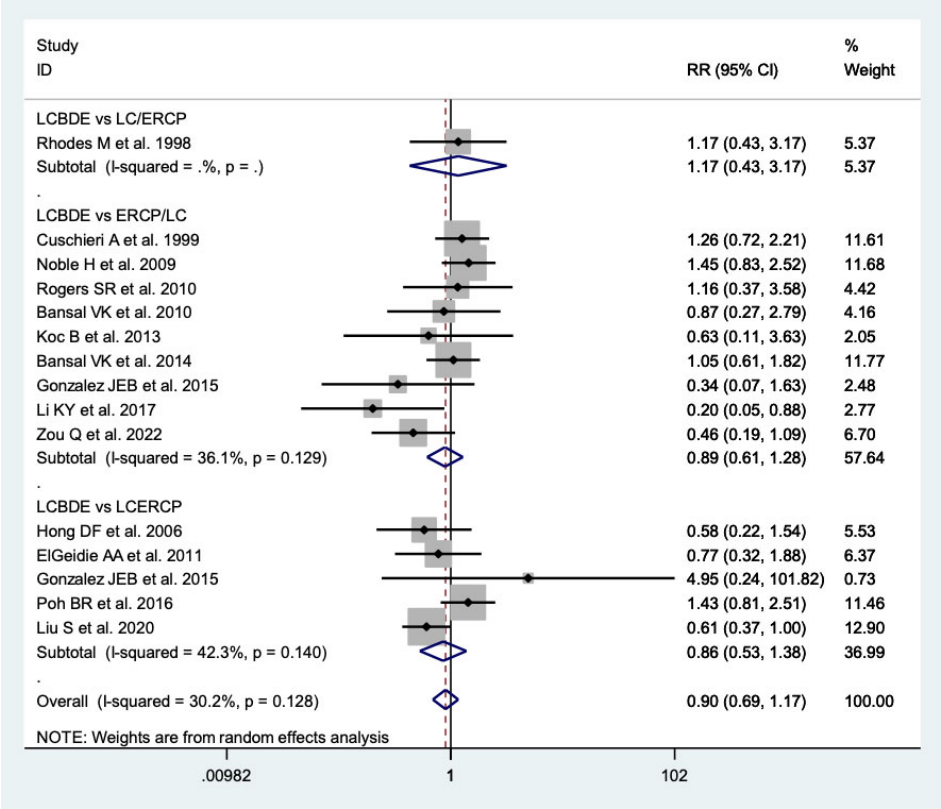

Figure 4. Forest plot for morbidity between LCBDE and LC+ERCP for treating gallstones with CBD stones.

The meta-analysis revealed that LC-LCBDE group obtained lower rate of mortality compared with LC+ERCP group, though the result had no significant differences (RR: 0.31; 95% CI: 0.06-1.55; **Supplementary Figure 2**).

Operative time

Eleven[19-21,23,25-31] of fourteen studies reported the operative time, and five[21,26,29-31] studies indicated the standard deviation of the mean. We can only perform a descriptive analysis of operative time instead of pooling the data. Three studies[19,25,27] showed longer operative time in LC-LCBDE group than that in LC+ERCP group, while the other eight studies[20,21,23,26,28-31] supported LC-LCBDE had shorter operative time.

Hospital stays

Thirteen of fourteen studies[16,19-21,23-31] reported the hospital stay, and three studies[21,29,31] indicated the standard deviation of the mean. We can only perform a descriptive analysis of hospital stay instead of pooling the data. For two-stage approaches, such as ERCP/LC and LC/ERCP, LC-LCBDE showed shorter hospital stay. A total of five studies[19,21,29-31] reported the comparison of LC-LCBDE and LCERCP on hospital stay, only Liu et al[30] supported LC-LCBDE had shorter hospital stay compared with LCERCP.

Cost

Six[21,24,27,29-31] of fourteen studies reported the cost for operation. All the studies supported LC-LCBDE had lower cost compared with LC+ERCP.

Meta-Analysis of Secondary Outcomes

Meta-analysis results of secondary outcomes were shown in Table IV. The results were as follows:

(1) Ten[16,19,21,23,26-31] of fourteen studies reported postoperative pancreatitis between two groups. LC-LCBDE group obtained lower rate of postoperative pancreatitis compared with LC+ERCP group. The result had significant differences (RR: 0.25; 95% CI: 0.13-0.46).

Table IV. Meta-analysis results of secondary outcomes.

Outcomes	No. of studies	Assessment of heterogeneity		No. of patients		Meta-analysis results	
		I^2 (%)	*p*	LCBDE	LC+ERCP	RR (95% CI)	*p*
Pancreatitis	10	0.0	0.721	1,013	957	0.25 (0.13-0.46)	<0.001
Bile leakage	12	0.0	0.993	918	860	4.52 (2.19-9.31)	<0.001
Cholangitis	5	0.0	0.965	473	470	0.17 (0.05-0.67)	<0.001
Hemorrhage	9	0.0	0.998	670	663	0.18 (0.07-0.42)	<0.001
Pneumonia	3	0.0	0.621	343	295	1.73 (0.61-4.88)	0.303
Surgical-site Infection	3	0.0	0.594	182	176	1.53 (0.42-5.61)	0.524
Conversion to open surgery	10	46.7	0.051	931	924	0.98 (0.45-2.11)	0.956

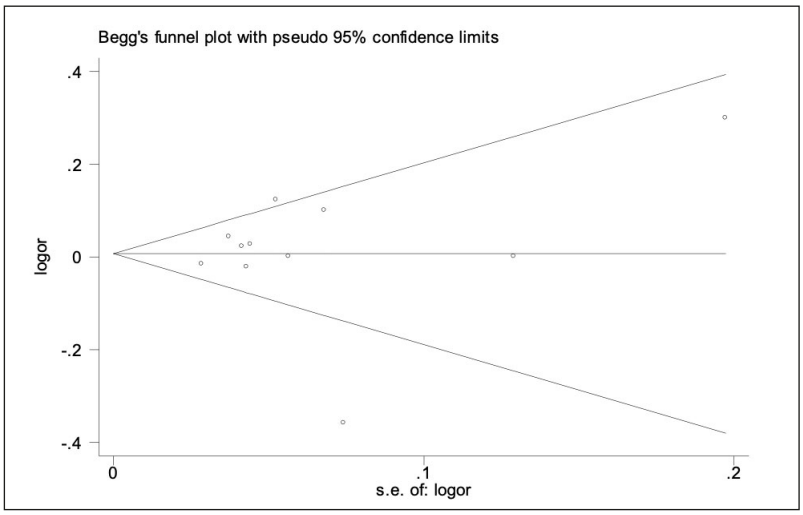

Figure 5. Funnel plot for publication bias evaluation.

(2) Eleven[19-21,23,25-31] of fourteen studies reported postoperative bile leakage between two groups. LC-LCBDE group obtained higher rate of postoperative bile leakage compared with LC+ERCP group. The result had significant differences (RR: 4.52; 95% CI: 2.19-9.31).
(3) Five[19,25,27,29,30] of fourteen studies reported postoperative cholangitis between two groups. LC-LCBDE group obtained lower rate of postoperative cholangitis compared with LC+ERCP group. The result had significant differences (RR: 0.17; 95% CI: 0.05-0.67).
(4) Nine[16,20,23,25-31] of fourteen studies reported postoperative hemorrhage between two groups. LC-LCBDE group obtained lower rate of postoperative hemorrhage compared with LC+ERCP group. The result had significant differences (RR: 0.18; 95% CI: 0.07-0.42).
(5) Three[16,21,28] of fourteen studies reported postoperative pneumonia between two groups. LC-LCBDE group obtained higher rate of postoperative pneumonia compared with LC+ERCP group. The result had no significant differences (RR: 1.73; 95% CI: 0.61-4.88).
(6) Three[23,25,28] of fourteen studies reported postoperative surgical-site infection between two groups. LC-LCBDE group obtained higher rate of postoperative surgical-site infection compared with LC+ERCP group. The result had no significant differences (RR: 1.53; 95% CI: 0.42-5.61).
(7) Eleven[16,19,20,22,23,25-30] of fourteen studies reported conversion to open surgery between two groups. LC-LCBDE group obtained lower rate of conversion to open surgery compared with LC+ERCP group. The result had no significant differences (RR: 0.98; 95% CI: 0.45-2.11).

Publication bias

Assessment of publication bias using Begg and Egger tests showed that there was no potential bias among the included studies (Begg test, p=0.484; Egger test, p=0.945; Figure 5).

Discussion

Open operation for CBD exploration has been abandoned because of severe injury to patients[32]. The main minimal-invasive approaches for CBD exploration are LCBDE and ERCP. However, the choice of the two techniques is always controversial with no current consensus[7]. ERCP used first to clean CBD stones and followed by LC is the main treatment strategy for concomitant gallbladder stones and CBD stones right now. However, this two-stage treatment strategy requires two anesthetic or hospital visits, which increase medical expenses, lengthen the duration of hospitalization, and add additional burden to patients[33]. An alternative strategy is to perform ERCP during the operation of LC, which overcomes the shortage of two-stage treatment. Sphincter of Oddi dysfunction (SOD) after ERCP has a high risk of post-ERCP pancreatitis and post-ERCP biliary complications, such as cholangitis and colicky pain[34]. LCBDE is considered as a safe way to retain the function of the sphincter of Oddi and does not increase the pressure of CBD during the treatment which results in lower rate of cholangitis and pancreatitis. However, LC-LCBDE also has its own disadvantages, such as higher rate of bile leakage, electrolyte disturbance and lower quality of life because of T-tube retaining. The latest con-

sensus guidelines[5,6], including those established by the European Society of Gastrointestinal Endoscopy and the American Society for Gastrointestinal Endoscopy[7], indicate that there is still insufficient evidence to establish the best approach for CBD stones.

The purpose of this meta-analysis was to compare the efficacy and safety of LC-LCBDE and LC+ERCP for patients with gallbladder stones and concomitant CBD stones. Our study indicated that, LC-LCBDE was associated with comparable effects compared with LC+ERCP in terms of surgical success rate, stone clearance rate, retained stones rate, operation time, and total morbidity. Two-stage treatment strategy has longer hospital stay compared with one-stage treatment. LC-LCBDE had lower cost compared with LC+ERCP. A further analysis showed that ERCP had higher rate of postoperative pancreatitis, cholangitis, and hemorrhage compared with LCBDE. At the same time, LCBDE had higher rate of bile leakage because of the T-tube retaining.

There are many complications due to biliary tract procedures. In the short term, it includes hemorrhage, pancreatitis, bile leakage, cholangitis, infection, perforation, and pneumonia. In the long term, it includes the stenosis of the Oddi sphincter, reflux of duodenal contents into the CBD, stone recurrence, and cholangiocarcinoma. The present study showed ERCP with higher rate of biliary-related complications, which is attributed to the procedure of the operation, such as endoscopic sphincterotomy (EST). The morbidity in ERCP group is always much more severe than LCBDE, which also result in a higher rate of mortality[35]. LCBDE is considered as a safer way to retain the function of the sphincter of Oddi and does not increase the pressure of CBD during the treatment. Compared with ERCP groups, LCBDE is a safer, visualizable, and controllable technique to deal with difficult CBD stones. The only limitation of LCBDE is the higher rate of bile leakage because of T-tube retaining and CBD suture performance[36]. As more and more surgeons[37] preferred to primary suture during LCBDE even for patients with acute cholangitis, T-tube retaining rate will greatly decrease in the future.

To the best of our knowledge, this is the most comprehensive meta-analysis based on 14 RCTs to compare the efficacy and safety of LCBDE and ERCP for CBD stones. There has been one published meta-analysis[14] based on 11 RCTs to analyze the differences of LCBDE and ERCP. In that study, the authors included two studies from the same institution, the same authors, and the same database, which impaired the reliability of the conclusion. They found there were no differences between LCBDE and ERCP in terms of detecting and removing CBD, and related complications. However, in this study, we found ERCP had significantly higher rate of pancreatitis, cholangitis and bleeding, and lower rate of bile leakage compared with LCBDE, which is consistent with published studies and related meta-analysis [4,9,33].

Limitations

There were several potential limitations in the study which should be considered. First, all included trials were not performed with double-blinded method, which might lead to selection bias. Second, the information of T-tube retaining or primary suture for LCBDE and operation position and whether to use the rendezvous technique for ERCP is unavailable in studies, which may have an impact on the results to some extent. Third, due to the limitation of the included studies, long-term outcomes, such as biliary stricture and cholangiocarcinoma were unavailable, it was not possible to make statistical comparisons of long-term effects between two groups.

Conclusions

This meta-analysis demonstrated that both LC+LCBDE and LC+ERCP are safe, effective, and minimal-invasive treatments for concomitant gallbladder and CBD stones. LC-LCBDE was associated with comparable effects compared with LC+ERCP in terms of surgical success rate, stone clearance rate, retained stones rate, operation time, and total morbidity. At the same time, LC-LCBDE had higher rate of bile leakage and lower rate of postoperative pancreatitis, cholangitis, and hemorrhage. More large-scale, well designed RCTs are needed to confirm our findings.

Funding

This study is supported by the Natural Science Foundation of Zhejiang Province. The grant number is LY19H160049.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this article.

Ethics Approval
This research is a meta-analysis of published research, there was no need for ethics approval.

Informed Consent
This research is a meta-analysis of published research, there was no need for the informed consent of patients.

Authors' Contributions
Lan and Li reviewed related articles and collected data from published research. Wang and Zhan checked the data from research independently to correct the possible mistakes. Yang and Wang analyzed the data and wrote the manuscript. Tang organized the total research.

ORCID ID
Kezhong Tang: 0000-0001-7844-606X.

References

1) Williams E, Beckingham I, El Sayed G, Gurusamy K, Sturgess R, Webster G, Young T. Updated guideline on the management of common bile duct stones (CBDS). Gut 2017; 66: 765-782.
2) Park CH. The Management of Common Bile Duct Stones. Korean J Gastroenterol 2018; 71: 260-263.
3) Cai JS, Qiang S, Bao-Bing Y. Advances of recurrent risk factors and management of choledocholithiasis. Scand J Gastroenterol 2017; 52: 34-43.
4) Lei C, Lu T, Yang W, Yang M, Tian H, Song S, Gong S, Yang J, Jiang W, Yang K, Guo T. Comparison of intraoperative endoscopic retrograde cholangiopancreatography and laparoscopic common bile duct exploration combined with laparoscopic cholecystectomy for treating gallstones and common bile duct stones: a systematic review and meta-analysis. Surg Endosc 2021; 35: 5918-5935.
5) Committee ASoP, Buxbaum JL, Abbas Fehmi SM, Sultan S, Fishman DS, Qumseya BJ, Cortessis VK, Schilperoort H, Kysh L, Matsuoka L, Yachimski P, Agrawal D, Gurudu SR, Jamil LH, Jue TL, Khashab MA, Law JK, Lee JK, Naveed M, Sawhney MS, Thosani N, Yang J, Wani SB. ASGE guideline on the role of endoscopy in the evaluation and management of choledocholithiasis. Gastrointest Endosc 2019; 89: 1075-1105 e15.
6) Testoni PA, Mariani A, Aabakken L, Arvanitakis M, Bories E, Costamagna G, Deviere J, Dinis-Ribeiro M, Dumonceau JM, Giovannini M, Gyokeres T, Hafner M, Halttunen J, Hassan C, Lopes L, Papanikolaou IS, Tham TC, Tringali A, van Hooft J, Williams EJ. Papillary cannulation and sphincterotomy techniques at ERCP: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy 2016; 48: 657-683.
7) Manes G, Paspatis G, Aabakken L, Anderloni A, Arvanitakis M, Ah-Soune P, Barthet M, Domagk D, Dumonceau JM, Gigot JF, Hritz I, Karamanolis G, Laghi A, Mariani A, Paraskeva K, Pohl J, Ponchon T, Swahn F, Ter Steege RWF, Tringali A, Vezakis A, Williams EJ, van Hooft JE. Endoscopic management of common bile duct stones: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy 2019; 51: 472-491.
8) Vannijvel M, Lesurtel M, Bouckaert W, Houben B, Knol J, Vangertruyden G, Sergeant G. A survey of European-African surgeons' management of common bile duct stones. HPB (Oxford) 2016; 18: 959-964.
9) Lin Y, Su Y, Yan J, Li X. Laparoendoscopic rendezvous versus ERCP followed by laparoscopic cholecystectomy in the management of cholecystocholedocholithiasis: a systemic review and meta-analysis. Surg Endosc 2020; 34: 4214-4224.
10) Muhammedoglu B. Single-stage treatment with ERCP and laparoscopic cholecystectomy versus two-stage treatment with ERCP followed by laparoscopic cholecystectomy within six to eight weeks: a retrospective study. Turk J Surg 2019; 35: 178-184.
11) Zhu J, Li G, Du P, Zhou X, Xiao W, Li Y. Laparoscopic common bile duct exploration versus intraoperative endoscopic retrograde cholangiopancreatography in patients with gallbladder and common bile duct stones: a meta-analysis. Surg Endosc 2021; 35: 997-1005.
12) Petelin JB. Laparoscopic approach to common duct pathology. Surg Laparosc Endosc 1991; 1: 33-41.
13) Zhen W, Xu-Zhen W, Nan-Tao F, Yong L, Wei-Dong X, Dong-Hui Z. Primary Closure Versus T-Tube Drainage Following Laparoscopic Common Bile Duct Exploration in Patients With Previous Biliary Surgery. Am Surg 2021; 87: 50-55.
14) Gao YC, Chen J, Qin Q, Chen H, Wang W, Zhao J, Miao F, Shi X. Efficacy and safety of laparoscopic bile duct exploration versus endoscopic sphincterotomy for concomitant gallstones and common bile duct stones: A meta-analysis of randomized controlled trials. Medicine (Baltimore) 2017; 96: e7925-e7934.
15) Cuschieri A, Croce E, Faggioni A, Jakimowicz J, Lacy A, Lezoche E, Morino M, Ribeiro VM, Toouli J, Visa J, Wayand W. EAES ductal stone study. Preliminary findings of multi-center prospective randomized trial comparing two-stage vs single-stage management. Surg Endosc 1996; 10: 1130-1135.
16) Cuschieri A, Lezoche E, Morino M, Croce E, Lacy A, Toouli J, Faggioni A, Ribeiro VM, Jakimowicz J, Visa J, Hanna GB. E.A.E.S. multicenter prospective randomized trial comparing two-stage vs single-stage management of patients with gallstone disease and ductal calculi. Surg Endosc 1999; 13: 952-957.
17) Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hrobjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S,

McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372: n71-n79.
18) 18: Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, McQuay HJ. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996; 17: 1-12.
19) Barreras Gonzalez JE, Torres Pena R, Ruiz Torres J, Martinez Alfonso MA, Brizuela Quintanilla R, Morera Perez M. Endoscopic versus laparoscopic treatment for choledocholithiasis: a prospective randomized controlled trial. Endosc Int Open 2016; 4: E1188-E1193.
20) Rhodes M, Sussman L, Cohen L, Lewis MP. Randomised trial of laparoscopic exploration of common bile duct versus postoperative endoscopic retrograde cholangiography for common bile duct stones. Lancet 1998; 351: 159-161.
21) Hong DF, Xin Y, Chen DW. Comparison of laparoscopic cholecystectomy combined with intraoperative endoscopic sphincterotomy and laparoscopic exploration of the common bile duct for cholecystocholedocholithiasis. Surg Endosc 2006; 20: 424-427.
22) Noble H, Tranter S, Chesworth T, Norton S, Thompson M. A randomized, clinical trial to compare endoscopic sphincterotomy and subsequent laparoscopic cholecystectomy with primary laparoscopic bile duct exploration during cholecystectomy in higher risk patients with choledocholithiasis. J Laparoendosc Adv Surg Tech A 2009; 19: 713-720.
23) ElGeidie AA, ElShobary MM, Naeem YM. Laparoscopic exploration versus intraoperative endoscopic sphincterotomy for common bile duct stones: a prospective randomized trial. Dig Surg 2011; 28: 424-431.
24) Rogers SJ, Cello JP, Horn JK, Siperstein AE, Schecter WP, Campbell AR, Mackersie RC, Rodas A, Kreuwel HT, Harris HW. Prospective randomized trial of LC+LCBDE vs ERCP/S+LC for common bile duct stone disease. Arch Surg 2010; 145: 28-33.
25) Bansal VK, Misra MC, Garg P, Prabhu M. A prospective randomized trial comparing two-stage versus single-stage management of patients with gallstone disease and common bile duct stones. Surg Endosc 2010; 24: 1986-1989.
26) Koc B, Karahan S, Adas G, Tutal F, Guven H, Ozsoy A. Comparison of laparoscopic common bile duct exploration and endoscopic retrograde cholangiopancreatography plus laparoscopic cholecystectomy for choledocholithiasis: a prospective randomized study. Am J Surg 2013; 206: 457-463.
27) Bansal VK, Misra MC, Rajan K, Kilambi R, Kumar S, Krishna A, Kumar A, Pandav CS, Subramaniam R, Arora MK, Garg PK. Single-stage laparoscopic common bile duct exploration and cholecystectomy versus two-stage endoscopic stone extraction followed by laparoscopic cholecystectomy for patients with concomitant gallbladder stones and common bile duct stones: a randomized controlled trial. Surg Endosc 2014; 28: 875-885.
28) Poh BR, Ho SP, Sritharan M, Yeong CC, Swan MP, Devonshire DA, Cashin PA, Croagh DG. Randomized clinical trial of intraoperative endoscopic retrograde cholangiopancreatography versus laparoscopic bile duct exploration in patients with choledocholithiasis. Br J Surg 2016; 103: 1117-1124.
29) Li KY, Shi CX, Tang KL, Huang JZ, Zhang DL. Advantages of laparoscopic common bile duct exploration in common bile duct stones. Wien Klin Wochenschr 2018; 130: 100-104.
30) Liu S, Fang C, Tan J, Chen W. A Comparison of the Relative Safety and Efficacy of Laparoscopic Choledochotomy with Primary Closure and Endoscopic Treatment for Bile Duct Stones in Patients with Cholelithiasis. J Laparoendosc Adv Surg Tech A 2020; 30: 742-748.
31) Zou Q, Ding Y, Li CS, Yang XP. A randomized controlled trial of emergency LCBDE + LC and ERCP + LC in the treatment of choledocholithiasis with acute cholangitis. Wideochir Inne Tech Maloinwazyjne 2022; 17: 156-162.
32) Jones DB, Soper NJ. The current management of common bile duct stones. Adv Surg 1996; 29: 271-289.
33) Singh AN, Kilambi R. Single-stage laparoscopic common bile duct exploration and cholecystectomy versus two-stage endoscopic stone extraction followed by laparoscopic cholecystectomy for patients with gallbladder stones with common bile duct stones: systematic review and meta-analysis of randomized trials with trial sequential analysis. Surg Endosc 2018; 32: 3763-3776.
34) Crittenden JP, Dattilo JB, Sphincter of Oddi Dysfunction. In StatPearls, Treasure Island (FL), 2022; 11: 132-139.
35) Desilets DJ. Management of post-ERCP complications. Minerva Chir 2017; 72: 157-168.
36) Al-Qudah G, Tuma F, T Tube. In StatPearls, Treasure Island (FL), 2022; 21: 187-196.
37) Zhou H, Wang S, Fan F, Peng J. Primary closure with knotless barbed suture versus traditional T-tube drainage after laparoscopic common bile duct exploration: a single-center medium-term experience. J Int Med Res 2020; 48: 300060519878087.