

# Laparoscopic Cholecystectomy and Endoscopic Retrograde Cholangiopancreatography (ERCP) in a One-Step Procedure in Comparison to the Standard Two-Step Procedure: A Systematic Review and Meta-Analysis

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**Background:** Current treatment of complicated calculous biliary disease typically involves a two-step procedure consisting of preoperative endoscopic retrograde cholangiopancreatography (ERCP) with or without CBD stents followed by laparoscopic cholecystectomy a few weeks later.

**Aim and objectives:** The aim of this study was to perform a systematic review & meta-analysis to study the effect of undergoing laparoscopic cholecystectomy and endoscopic retrograde cholangiopancreatography (ERCP) in the same session versus different sessions.

**Patients and methods:** This is a systematic review & meta-analysis. A total of 1054 citations were obtained for title and abstract review. Of the 1054 citations, 118 duplicates were removed with the Endnote X5 software, and 926 irrelevant studies were excluded by scanning the titles and abstracts. Full texts of the remaining 10 eligible studies were retrieved for review.

**Results:** Mean Total cost per patient was 45,157.15 US Dollars (USD) in single stage vs 52,486.6 USD in two stages group, ERCP success was 335/351 (95.4%) in single stage vs 528/572 (92.3%) in two stage group, failure was found in 7/243 (2.8%) in single stage vs 13/347 (3.7%) two stage group and repeat ERCP required in 4/336 (1.2%) in one stage group while 17/342 (4.9%) in two stage group. Bile leak found in 8/325 (2.5%) single stage vs 7/428 (1.6%) in two stage groups.

**Conclusion:** The present meta-analysis showed that combining Laparoscopic Cholecystectomy and Endoscopic Retrograde Cholangiopancreatography (ERCP) in a one-step procedure had the advantages of shorter procedural duration, less hospital stay, lower cost and lower complication rate in comparison to two stage procedure, however both stage procedures have similar success rates. Another advantage of the one-stage procedure is clearing the CBD and removing the gall bladder at the same time so CBD stents would not be required to be inserted and removed in another session later. However, one-stage procedure is not feasible in all hospitals due to required preparations of the Operations Room in contrast to the two-stage procedure.

**Key words:** Cholecystectomy, Choledocholithiasis, Endoscopic retrograde cholangiopancreatography (ERCP), GI endoscopy, One-step, Two-step.

## Introduction

A gallstone is a stone formed within the gallbladder out of precipitated bile components. The term cholelithiasis may refer to the presence of gallstones or to any disease caused by gallstones, and choledocholithiasis refers to presence of migrated gallstones within bile ducts.<sup>1</sup>

Most people with gallstones (About 80%) are asymptomatic. However, when a gallstone obstructs the bile duct it causes acute cholestasis, resulting in a biliary colic. This happens in 1–4% of those with gallstones each year. Complications of gallstones may include cholecystitis, pancreatitis, obstructive jaundice, and cholangitis. Symptoms of these complications may include prolonged pain, fever, yellowish skin, vomiting, dark urine, and pale stools.<sup>2</sup>

Laparoscopic cholecystectomy is the gold standard for surgical treatment of calcular gall bladder. The number of laparoscopic cholecystectomies performed has increased significantly. On the other

hand, ERCP is used primarily to diagnose and treat conditions of the bile ducts and main pancreatic duct, including gallstones.<sup>3</sup>

The current standard two-step surgical treatment of a patient with impacted stone in the common bile duct (CBD stone) associated with gall bladder stones is to perform ERCP first and remove the stone. A few weeks later laparoscopic cholecystectomy (LC) would be arranged to prevent further attacks.<sup>1</sup> If the LC would be delayed or the CBD is not fully cleared of all impacted stones, a CBD stent would be inserted, to be later removed in another session later.

Approximately 5% to 15% of patients with gallstones have concomitant (CBD) stones.<sup>4</sup> As the debate on the optimal choice for these patients is ongoing, surgeons are often bewildered by the variety of therapies which have emerged in the minimally invasive era. Many surgeons believe a combination of endoscopic stone extraction and LC would be the next gold standard method.<sup>5</sup>

However, there are a few studies which address the benefits of one-step procedure of laparoscopic cholecystectomy (LC) and ERCP over the standard two-step procedure. Moreover, the results of these studies are conflicting.

### **Aim of the Work**

The aim of this study is to perform a systematic review & meta-analysis to study the effect of undergoing laparoscopic cholecystectomy and endoscopic retrograde cholangiopancreatography (ERCP) in the same session versus different sessions.

### **Patients and methods**

This was a systematic review & meta-analysis. A total of 1054 citations were obtained for title and abstract review. Of the 1054 citations, 118 duplicates were removed with the Endnote X5 software, and 926 irrelevant studies were excluded by scanning the titles and abstracts. Full texts of the remaining 10 eligible studies were retrieved for review.

### **Criteria for considering studies for this review:**

#### **Types of studies:**

- Systematic review and meta-analysis.
- Randomized controlled studies.

#### **Types of participants:**

- Only studies on human subject with impacted stone in the common bile duct (CBD stone) associated with gall bladder stones will be included.

#### **Types of interventions:**

##### **Operative interventions either:**

- ERCP.
- Laparoscopic cholecystectomy (LC).

##### **Types of outcome measures:**

- Total Operative Time.
- Preoperative days
- Length of Hospital Stay.
- Hospital Costs
- Additional procedures
- **Safety including:**
  1. Complications (Incisional infection, bleeding, Fever, Pulmonary infection and Acute pancreatitis).
  2. Failure rate

### **Selection criteria for studies:**

The inclusion criteria were English studies, patients with gall bladder stones and/or common bile duct stones and operative interventions either ERCP or laparoscopic cholecystectomy (LC). While the exclusion criteria regarding types of studies were: Case series studies and case report studies; also, types of participants: Previous abdominal surgical intervention and GIT tumors.

Search strategy for identification of studies: The search was conducted by using the databases: MEDLINE, PubMed, Google scholarship, The Cochrane Collaboration, using the following keywords: "gall bladder stones", "ERCP", "laparoscopic cholecystectomy", "common bile duct stones" or published studies from 2015-2021.

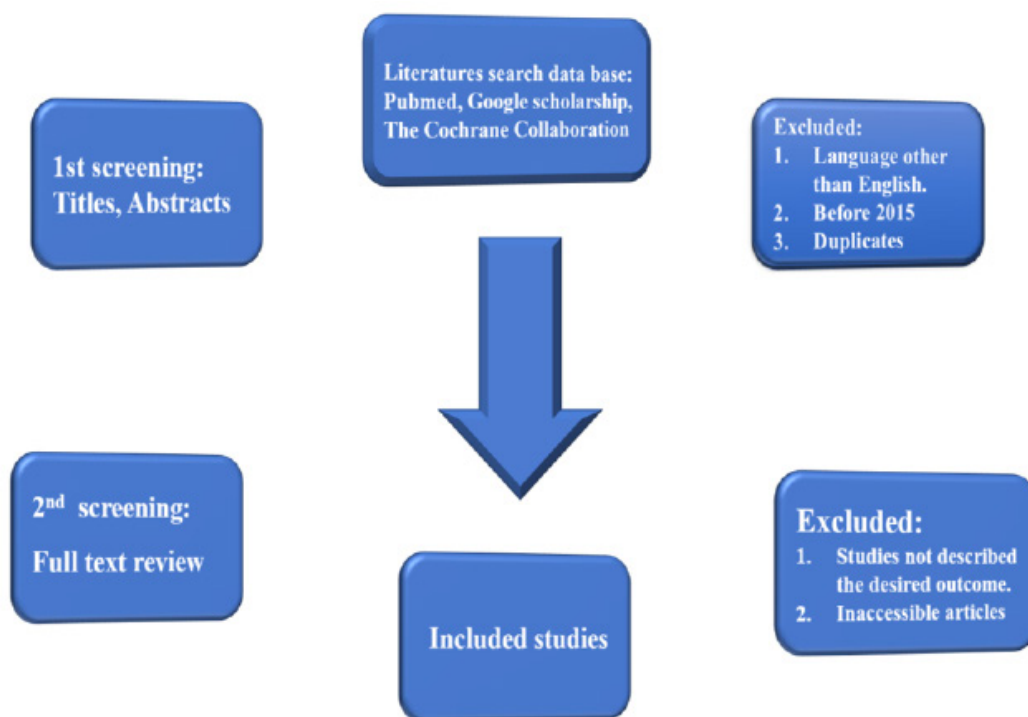
### **Methods of the review**

- **Locating and selecting studies:** Abstracts of articles identified using the above search strategy were viewed, and articles that appear to fulfill the inclusion criteria were being retrieved in full, when there is a doubt, a second reviewer will assess the article and consensus were being reached.
- **Data extraction:** Data were being independently extracted by two reviewers and cross-checked.
- **Statistical considerations:** Outcomes from included trials were combined using the systematic review manager software and manually screened for eligibility to be included. PRISMA flowchart were produced based on the search results and the inclusion/exclusion criteria.
- After pooling of the collected data from the desired search studies, the relative risk of each of the-intended outcome measures of interest were calculated and compared between each of ERCP & laparoscopic cholecystectomy in management of gall bladder stones aiming to reach a satisfactory conclusion.
- **Publication bias:** Risk of bias assessment for all included studies using Cochrane risk of bias-assessment tool.

### **Results**

#### **Search results**

A total of 1054 citations were obtained for title and abstract review (**Fig. 1**). Of the 1054 citations, 118 duplicates were removed with the Endnote X5 software, and 926 irrelevant studies were excluded by scanning the titles and abstracts. Full texts of the remaining 10 eligible studies were retrieved for review.



**Fig 1: PRISMA "Preferred Reporting Items for Systematic Reviews and Meta-analysis" flow diagram for study selection.**

### Study characteristics

10 studies were included; 5 were prospective and 5 were retrospective as shown in **(Table 1)**.

### Patient's characteristics

1312 cases were included, mean age was 55.3 years 527 cases were single stage and 785 were two stages as shown in **(Table 2)**.

### Patient's history

Main complains were Abdominal pain, Fever, Abdominal distension, Nausea/vomiting, Jaundice, biliary symptoms, pruritis, Cholangitis and Pancreatitis. The mean Charlson Comorbidity Index CCI (A weighted index to predict risk of death within 1 year of hospitalization for patients with specific comorbid conditions. It's derived by summing the assigned weights of all comorbid conditions presented by the client. Higher scores indicate a more severe condition and consequently, a worse prognosis) was 1.85 in single stage group vs 1.4 in two stages group, as regard co morbidities mainly was DM,HTN, COPD, Coronary artery disease, renal, pulmonary, cardiovascular as shown in **(Table 3)**.

### Operative history

Mean operative time was 100.4 in single stage vs 120.7 in two stages group, mean length of stay (LOS) was 5.1 in single stage vs 6.46 in two stages

and as regard estimated blood loss (EBL) was 51.05 in single stage vs 46.25 two stages group as shown in **(Table 4)**.

### Outcome

Mean Total cost per patient was 45,157.15 USD in single stage vs 52,486.6 USD in two stages group, ERCP success was 335\351 (95.4%) in single stage vs 528\572 (92.3%) in two stage group, failure was found in 7\243 (2.8%) in single stage vs 13\347 (3.7%) two stage group and repeat ERCP required in 4\336 (1.2%) in one-stage group and in 17\342 (4.9%) in two stage group.

Bile leak found in 8\325 (2.5%) single stage vs 7\428 (1.6%) in two stage group as showed in **(Table 5)**.

### Complications

Complications found in 14\527 (2.2%) in single stage group and were in the form of infection in 4 cases, pancreatitis in 4 cases, intraabdominal abscess, minor bleeding in 2 cases, residual stone in 1 case and 28\785 (3.6%) in two stage in form of pancreatitis in 7 cases, intraabdominal abscess in 3 cases, duodenal perforation in 2 cases, bleeding in 5 cases, infection in 6 cases, ileus in 1 case, residual stones in 4 cases as shown in **(Table 6)**.

**Table 1: Study characteristics**

Author	Type of study
Yan Y et al., 2022	Retrospective
Hassan AM et al., 2021	Prospective
Muhammedoğlu B et al., 2020	Prospective
Zhou Y et al., 2019	Retrospective
RADY M et al., 2019	Prospective
AL-TEMIMI MH et al., 2018	Retrospective
Selimah MF et al., 2016	Prospective
Lv F et al., 2016	Prospective
Mallick R et al., 2016	Retrospective
Wild JL et al., 2015	Retrospective

**Table 2: Patient's characteristics**

Author		Number	Age	m\ f
Yan Y et al.,2022	single stage	28	65	15\ 13
	two stage	32	67	17\ 15
Hassan AM et al.,2021	single stage	50	46.2	10\ 40
	two stage	50	48.2	5\ 45
Muhammedoğlu B et al.,2020	single stage	39	62	-
	two stage	37	54	-
Zhou Y et al.,2019	single stage	54	-	29\ 25
	two stage	46	-	26\ 20
RADY M et al.,2019	single stage	25	47.24	20\ 4
	two stage	25	44.76	20\ 5
AL-TEMIMI MH et al.,2018	single stage	164	47.5	58\ 106
	two stage	276	52.1	96\ 180
Selimah MF et al.,2016	single stage	40	52.1	15\ 25
	two stage	40	53.1	11\  29
Lv F et al.,2016	single stage	29	61.3	20\ 9
	two stage	24	63.5	15\ 9
Mallick R et al.,2016	single stage	33	49	-
	two stage	80	52.1	-
Wild JL et al.,2015	single stage	65	65	24\ 41
	two stage	175	66	81\ 94

**Table 3: Patient's history**

Author		Complaint	Charlson Comorbidity Index	Co morbidities
Yan Y et al., 2022	Single stage	Abdominal pain, Fever, Abdominal distension, Nausea/vomiting, Jaundice	N/A	DM, HTN, COPD, Coronary artery disease
	Two stage	Abdominal pain, Fever, Abdominal distension, Nausea/vomiting, Jaundice	N/A	DM, HTN, COPD, Coronary artery disease
Hassan AM et al., 2021	Single stage	N/A	N/A	N/A
	Two stage	N/A	N/A	N/A
Muhammedoğlu B et al., 2020	Single stage	N/A	N/A	N/A
	Two stage	N/A	N/A	N/A
Zhou Y et al., 2019	Single stage	jaundice, biliary symptoms	1.85	HTN, DM, COPD
	Two stage	jaundice, biliary symptoms	1.8	HTN, DM, COPD
RADY M et al., 2019	Single stage	Right upper quadrant pain, Jaundice, Pruritus, Fever, Nausea and vomiting,	N/A	N/A
	Two stage	Right upper quadrant pain, Jaundice, Pruritus, Fever , Nausea and vomiting, Cholangitis, Pancreatitis	N/A	N/A
AL-TEMIMI MH et al., 2018	Single stage	N/A	N/A	N/A
	Two stage	N/A	N/A	N/A
Selimah MF et al., 2016	Single stage	N/A	N/A	N/A
	Two stage	N/A	N/A	N/A
Lv F et al., 2016	Single stage	N/A	N/A	N/A
	Two stage	N/A	N/A	N/A
Mallick R et al., 2016	Single stage	Abdominal pain, Jaundice. Nausea/vomiting	N/A	N/A
	Two stage	Abdominal pain, Jaundice, Nausea/vomiting	N/A	N/A
Wild JL et al., 2015	Single stage	NA	0	HTN, DM, renal, pulmonary, cardiovascular
	Two stage	NA	1	HTN, DM, renal, pulmonary, cardiovascular

**Table 4: Operative history**

Author		Operative time (minutes)	LOS	EBL (mL)
Yan Y et al., 2022	single stage	161±56	12±5	80±25
	two stage	132±50	11±4	70±30
Hassan AM et al., 2021	single stage	40±10.4	2±1	-
	two stage	75.4±16.8	5.4±3.2	-
Muhammedoğlu B et al., 2020	single stage	90	7	-
	two stage	110	8	-
Zhou Y et al., 2019	single stage	-	6.2(2,2)	-
	two stage	-	6(2.1)	-
RADY M et al., 2019	single stage	99.2	4.44	-
	two stage	226.4	4.92	-
AL-TEMIMI MH et al., 2018	single stage	-	2.99 ± 2.34	22.1 ± 29.1
	two stage	-	3.84 ± 2.52	22.5 ± 37.2
Selimah MF et al., 2016	single stage	82.7	2.85±1.42	-
	two stage	70.1	3.33±1.28	-
Lv F et al., 2016	single stage	-	6.72 ± 1.3	
	two stage	-	10.91 ± 1.6	
Mallick R et al., 2016	single stage	142 ± 58	4.8 ± 2.6	-
	two stage	142 ± 64	6.2 ± 3.3	-
Wild JL et al., 2015	single stage	88	3	-
	two stage	89	5	-

**Table 5: Outcome**

Author		Total cost per patient (USD)	ERCP success	Failure	Repeat ERCP	Bile leak
Yan Y et al., 2022	Single stage	45956.7 ±10524.6	27	-	-	1
	two stage	52162.2±12059.3	30	-	-	0
Hassan AM et al., 2021	Single stage	-	-	-	0	0
	two stage	-	-	-	11	3
Muhammedoğlu B et al., 2020	Single stage	2141.93	-	-	-	-
	two stage	2760.61	-	-	-	-
Zhou Y et al., 2019	Single stage	-	-	2	-	6
	two stage	-	-	5	-	0
RADY M et al., 2019	Single stage	-	20	5	-	-
	two stage	-	19	6	-	-
AL-TEMIMI MH et al., 2018	Single stage	-	164	0	-	0
	two stage	-	258	2	-	1
Selimah MF et al., 2016	Single stage	-	31	-	-	-
	two stage	-	31	-	-	-
Lv F et al., 2016	Single stage	15,724 ± 1613	28	-	-	1
	two stage	19,829 ± 2433	24	-	-	3
Mallick R et al., 2016	Single stage	42261 ± 23238	-	-	-	-
	two stage	49276±24481	-	-	-	-
Wild JL et al., 2015	Single stage	90,269	65	-	4	-
	two stage	102,537	166	-	6	-

**Table 6: Complications**

Author		Compli- cations	Pan- creati- tis	Intra-ab- dominal abscess	Duodenal perfora- tion	Bleed- ing	Infec- tion	Medical complica- tions	Ile- us	Re- sidual stones
Yan Y et al., 2022	Single Stage	<b>2</b>	0	0	0	0	<b>2</b>	0	0	0
	Two Stage	<b>3</b>	<b>2</b>	0	0	0	<b>1</b>	0	0	0
Hassan AM et al., 2021	Single Stage	<b>2</b>	0	0	0	0	<b>2</b>	0	0	0
	Two Stage	<b>5</b>	0	0	0	0	<b>5</b>	0	0	0
Muhammedoğlu B et al., 2020	Single Stage	<b>0</b>	0	0	0	0	0	0	0	0
	Two Stage	<b>0</b>	0	0	0	0	0	0	0	0
Zhou Y et al., 2019	Single Stage	<b>0</b>	0	0	0	0	0	0	0	0
	Two Stage	<b>6</b>	<b>2</b>	0	<b>1</b>	<b>1</b>	0	0	0	<b>2</b>
RADY M et al., 2019	Single Stage	<b>0</b>	0	0	0	0	0	0	0	0
	Two Stage	<b>0</b>	0	0	0	0	0	0	0	0
AL-TEMIMI MH et al., 2018	Single Stage	<b>7</b>	<b>2</b>	<b>1</b>	0	<b>2</b>	0	<b>2</b>	0	0
	Two Stage	<b>10</b>	<b>1</b>	<b>3</b>	<b>1</b>	<b>4</b>	0	0	<b>1</b>	0
Selimah MF et al., 2016	Single Stage	<b>1</b>	<b>1</b>	0	0	0	0	0	0	0
	Two Stage	<b>2</b>	<b>2</b>	0	0	0	0	0	0	0
Lv F et al., 2016	Single Stage	<b>1</b>	0	0	0	0	0	0	0	<b>1</b>
	Two Stage	<b>2</b>	0	0	0	0	0	0	0	<b>2</b>
Mallick R et al., 2016	Single Stage	<b>0</b>	0	0	0	0	0	0	0	0
	Two Stage	<b>0</b>	0	0	0	0	0	0	0	0
Wild JL et al., 2015	Single Stage	<b>1</b>	<b>1</b>	0	0	0	0	0	0	0
	Two Stage	<b>0</b>	0	0	0	0	0	0	0	0

## Discussion

Acute cholecystitis (AC) is a very common inflammatory disease of the gallbladder and the most common complication of gallstone disease, as well as 95% of AC patients is associated with cholecystolithiasis.<sup>6</sup> Cholecysto-choledocholithiasis refers to the simultaneous presence of stones in the gallbladder and the common bile duct (CBD). The incidence of concomitant choledocholithiasis in patients with cholecystolithiasis has been reported

to range between 10% and 20% depending on geographic distribution.<sup>7</sup>

The frequency of CBD stones complicating AC range between 7.7% and 14.3%.<sup>8,9</sup> Following the recent guideline, early or urgent LC is recommended for patients with AC who are deemed capable of withstanding surgery regardless of exactly how much time has passed since symptoms onset.<sup>13-17</sup> Even though LC appears to be a safe treatment option for patients with AC, the concomitant CBD

stones demand proper treatment and may cause severe complications in the absence of immediate treatment.<sup>18</sup>

While both one-stage and two-stage therapeutic strategies are considered equally safe and feasible for management of concomitant CBD stones and gallstone, there are very few studies provided insights into the advisability and timing of management of AC associated with CBD stones.

However, it is still unclear whether laparoscopic cholecystectomy (LC) plus ERCP in a single-stage is superior to LC with ERCP in two-stages. Therefore, we conducted this meta-analysis to study the effect of performing laparoscopic cholecystectomy and endoscopic retrograde cholangiopancreatography (ERCP) in the same session versus different sessions.

This current systematic review and meta-analysis included 10 eligible studies Yan et al.,<sup>20</sup> Hassan et al.,<sup>21</sup> Muhammedoğlu et al.,<sup>22</sup> Zhou et al.,<sup>23</sup> Rady et al.,<sup>24</sup> AL-Temimi et al.,<sup>25</sup> Selimah et al.,<sup>26</sup> Lv F et al., (2016), Mallick et al.,<sup>27</sup> Wild et al.,<sup>28</sup> out of them there were five studies retrospective (Yan et al.,<sup>20</sup> Zhou et al.,<sup>23</sup> AL-Temimi et al.,<sup>25</sup> Mallick et al.,<sup>27</sup> Wild et al.,<sup>28</sup>) and five prospective studies (Hassan et al.,<sup>21</sup>; Muhammedoğlu et al.,<sup>22</sup> Rady et al.,<sup>24</sup> Selimah et al.,<sup>26</sup> Lv F et al.,<sup>29</sup>), with total number of 1312 patients. There was a total of 527 patients were operated with single stage procedure while there were 785 patients were operated by two-staged procedure.

The pooled data showed that the mean age of patients was 55.3 years, with predominance of female's 59.9% and 41.1% males.

Regarding complain, it was reported by 4 studies [Yan et al.,<sup>20</sup> Zhou et al.,<sup>23</sup> Rady et al.,<sup>24</sup> Mallick et al.,<sup>27</sup>

World Society of Emergency Surgery guidelines Ansaloni et al.,<sup>30</sup> reported that most people with gallstones (About 80%) are asymptomatic. However, when a gallstone obstructs the bile duct and causes acute cholestasis, resulting in a biliary colic. This happens in 1–4% of those with gallstones each year. Complications of gallstones may include cholecystitis, pancreatitis, obstructive jaundice, and cholangitis. Symptoms of these complications may include prolonged pain, fever, yellowish skin, vomiting, dark urine, and pale stools.

Regarding Charlson Comorbidity Index, it was reported by two studies [Zhou et al.,<sup>23</sup>; Wild et al.,<sup>28</sup>] with mean value of was 1.1625.

The Charlson Comorbidity Index (CCI) was developed and validated as a measure of 1-year mortality risk and burden of disease. To account for age being an

independent predictor of mortality, a Combined Age-CCI (CA-CCI) score can be generated. The CCI has been extensively used in clinical research to address the confounding influence of comorbidities, predict outcomes, standardize comorbidities abstracted from medical records or administrative databases and for self-report of comorbidities. In clinical practice, the CCI reduces comorbidities into a single numeric score that may assist health professionals with stratifying patients into subgroups based on disease severity, developing targeted models of care and resource allocation.<sup>31</sup>

As regard comorbidities, it was reported that the most common comorbidities were DM and HTN as reported in three studies [Yan et al.,<sup>20</sup>; Zhou et al.,<sup>23</sup> Wild et al.,<sup>28</sup>].

Regarding operative time, it was reported that the single stage surgery takes significantly longer surgical time compared to two-stage surgery as reported by Yan et al.,<sup>20</sup> & AL-Temimi et al.,<sup>25</sup> however other studies stated that the single stage surgery take significantly shorter surgical time compared to two-stage surgery as reported by [Hassan et al.,<sup>21</sup> Muhammedoğlu et al.,<sup>22</sup> Rady et al.,<sup>24</sup>

While some studies reported that there was no significant difference in surgery time between both procedures as reported by [Mallick et al.,<sup>32</sup> Wild et al.,<sup>28</sup>].

The pooled data showed that the average operative time for single-stage procedure was 100.4 min and for two-stage procedure was 120.6 min.

It was reported that intraoperative ERCP+LC is more complicated, resulting in a longer operation time.<sup>33</sup>

In agreement with the current study Zhu et al.,<sup>34</sup> performed a meta-analysis on 8 RCTs aimed to evaluate the safety and effectiveness of single-stage [laparoscopic cholecystectomy (LC) + laparoscopic common bile duct exploration (LCBDE)] vs. two-stage management [preoperative endoscopic retrograde cholangiopancreatography (ERCP) + LC] for concomitant gallstones and common bile duct stones. The meta-analysis showed that the lengths of total operative time (MD = -16.78, 95% CI: -27.55 to -6.01, P = 0.002) was shorter in the single-stage group.

However, the meta-analysis by Li et al.,<sup>16</sup> aimed to compare the effectiveness and safety of single-stage (laparoscopic cholecystectomy [LC] plus laparoscopic common bile duct exploration [LCBDE]) with two-stage (LC plus endoscopic retrograde cholangiopancreatography (ERCP)/ endoscopic sphincterotomy [EST]) in management for concomitant gallstones and common bile duct (CBD) stones, including 11 studies and revealed



that there was no statistically significant difference in operative time between both procedures.

Similar meta-analysis by Prasson et al,<sup>35</sup> showed that there was no statistically significant difference in operative time between both procedures.

Regarding length of hospital stay, it was reported by all the included studies, by pooling all data it was revealed that the hospital stay was significantly longer in two-stage procedure (6.4 day) compared to single stage. (5.2 day).

This was agreed with the results of the meta-analysis by Liao et al,<sup>36</sup> who revealed that the length of hospital stay was shorter in the single stage group (MD=-2.75, P<.05) compared to two-stage group.

Also, in concordance with the present study the meta-analysis by Tan et al.<sup>37</sup> showed that the mean days of hospital stay for single stage group (M = 3.52, SD = 1.434, N = 5) was significantly less than the two-stage group (M = 6.10, SD = 2.074, N = 5), t (8) = 2.29, p< 0.05).

As well, Zhu et al,<sup>34</sup> showed that the lengths of hospital stay (MD = -1.02, 95% CI: -1.99 to -0.04, P = 0.04) was shorter in the single-stage group.

However, the meta-analyses by Li et al,<sup>16</sup> revealed that no significant difference was noted between the two groups length of hospital stay (WMD: 1.24, 95% CI: 3.57-1.09, P = 0.30).

Similar meta-analysis by Prasson et al,<sup>35</sup> showed that there was no statistically significant difference in length of hospitalization between both procedures.

Regarding estimated blood loss volume, it was reported by two studies Yan et al,<sup>20</sup> reported that the single stage procedure has higher amount of blood loss compared to two staged procedures, however, AL-Temimi et al,<sup>25</sup> revealed that the blood loss was similar in both procedures.

As regard cost effectiveness, it was reported by five studies [Yan et al,<sup>20</sup> Muhammedoğlu et al,<sup>22</sup> Lv F et al,<sup>29</sup> Mallick et al,<sup>32</sup> Wild et al,<sup>28</sup>] all studies reported that the single stage procedure was better than two-staged procedure in terms of cost effectiveness.

This was agreed with Kenny et al,<sup>38</sup> who reviewed several meta-analysis studies comparing the advantages of one stage LC +LCBDE to the 2 stage ERCP + LC, which showed equivalent clinical complications but better cost-effectiveness due to reduced length of hospital stay. The paper concluded LC + LCBDE to be the preferred procedure where resources and local expertise are available. This study highlights the advantage of LC +LCBDE as a one stage procedure, not the advantage of LCBDE as the surgical technique itself.

As well, the meta-analysis by Zhu et al,<sup>34</sup> showed that the single-stage (LC + LCBDE) management approach treats both gallstones and CBDs in a single-stage and is cost-effective with shorter hospital stays.

Regarding ERCP success, it was reported by six studies [Yan et al,<sup>20</sup> Rady et al,<sup>24</sup> AL-Temimi et al,<sup>25</sup> Selimah et al,<sup>26</sup> Lv F et al,<sup>29</sup> Wild et al,<sup>28</sup>]. In single stage procedure the total success was found in 335\351 (95.4%) patients while in two-stage procedure there were 528\572 (92.3%) patients.

Regarding failures, it was reported by three studies [Zhou et al,<sup>23</sup> Rady et al,<sup>24</sup> AL-Temimi et al,<sup>25</sup>], in single stage procedure the total failures was found in 7\243 (2.8%) patients while in two-stage procedure there were 13\347 (3.7%) patients.

Regarding ERCP reoperations, it was reported by two studies [Hassan et al,<sup>21</sup> Wild et al,<sup>28</sup>], in single stage procedure the total reoperations was found in 4\336 (1.2%) patients while in two-stage procedure there were 17\342 (4.9%) patients.

Regarding bile leak, it was reported by five studies, [Yan et al,<sup>20</sup> Hassan et al,<sup>21</sup> Zhou et al,<sup>23</sup> AL-Temimi et al,<sup>25</sup> Lv F et al,<sup>29</sup>]. In single stage procedure the total bile leak was found in 8\325 (2.4%) patients while in two-stage procedure there were 7\428 (1.0%) patients.

The current study showed no significant difference in success rate between both groups this was agreed with the meta-analyses by Liao et al, (36) who revealed that no significant difference was noted between the two groups regarding CBD stone clearance (RR=1.03, P=.27), postoperative papilla bleeding (RR=0.41, P=.13), postoperative cholangitis (RR=0.87, P=.79), and operation conversion rate (RR=0.71, P=.26).

Also, the meta-analysis by Li et al,<sup>16</sup> showed that no significant difference was noted between the two groups regarding CBD stone clearance (RR: 1.06; 95% CI: 0.99-1.14; P = 0.12), retained stone (RR: 0.91; 95% CI: 0.57-1.47; P = 0.71), conversion to other procedures (RR: 0.80; 95% CI: 0.55-0.16; P = 0.23), length of hospital stay (WMD: 1.24, 95% CI: 3.57-1.09, P = 0.30), total operating time (WMD: 25.42, 95% CI: 22.38-73.22, P = 0.30).

As well, the meta-analyses by Tan et al,<sup>37</sup> showed that the success rate of CBD clearance (Single stage = 93%, two stage = 92%) was the same in both groups (OR 1.34; 95% CI 0.45-0.97; p = 0.60).

Similarly, the meta-analysis by Prasson et al,<sup>35</sup> showed that there is no significant difference between the two arms regarding successful CBD stone clearance (RR = 0.96, P = 0.15).

Furthermore, a meta-analysis by Alexakis et al,<sup>39</sup> compared one- and two-stage laparoscopic/endoscopic management of common bile duct stones, 9 trials with 933 patients were studied. No significant difference was observed between the two groups regarding bile duct clearance (OR, 0.89; 95% CI, 0.65–1.21).

However, the meta-analysis by Zhu et al,<sup>34</sup> revealed that the common bile duct stone clearance rate in the single-stage group was higher (OR = 1.56, 95% CI: 1.05 to 2.33, P = 0.03).

The overall complications rate was (2.46%) in single stage procedure and (3.56%) in two stage procedure; Pancreatitis (0.76% vs. 0.9% in single- vs. two-stage respectively), Intra-abdominal abscess (0.37% vs. 0.38% in single- vs. two-stage respectively), Duodenal perforation (0% vs. 0.25% in single- vs. two-stage respectively), Bleeding, infection (0.37% vs. 0.64% in single- vs. two-stage respectively), Medical complications (0.37% vs. 0.76% in single- vs. two-stage respectively), Ileus (0% vs. 0.12% in single- vs. two-stage respectively) and residual stones (0.19% vs. 0.51% in single- vs. two-stage respectively).

Our results were supported by the meta-analyses by Liao et al.,<sup>36</sup> revealed that the single stage procedure was associated with lower overall morbidity (RR= 0.54, P<.05), postoperative pancreatitis (RR=0.29, P<.05) and cannulation failure rate (RR=0.22, P<.05).

Also, the meta-analyses by Tan et al,<sup>37</sup> showed that single stage was associated with less pancreatitis (0.6%) than two-stage (4.4%) (OR 0.19; 95% CI 0.06–0.67; p = 0.01; 2I = 43%). The incidence of overall morbidity was lower in the single stage group (6%) than the two-stage group (11%) (OR 0.54; 95% CI 0.31–0.96; p = 0.03; I2 = 20%).

However, the meta-analysis by Li et al,<sup>16</sup> showed that no significant difference was noted between the two groups regarding post-operative morbidity (RR: 1.03; 95% CI: 0.79–1.34; P = 0.81) and mortality (RR: 0.30; 95% CI: 0.06–1.41; P = 0.13).

As well, the meta-analysis by Zhu et al,<sup>34</sup> revealed that there was no statistically significant difference between the two groups regarding postoperative morbidity (OR = 1.12, 95% CI: 0.79 to 1.59, P = 0.52), mortality (OR = 0.29, 95% CI: 0.06 to 1.41, P = 0.13) and conversion to other procedures (OR = 0.82, 95% CI: 0.37 to 1.82, P = 0.62).

Similarly, the meta-analysis by Prasson et al,<sup>35</sup> showed that there is no significant difference between the two arms mortality (RR = 1.74, P = 0.33), morbidity (RR = 0.89, P = 0.32), conversion to additional procedure (RR = 1.44, P = 0.09),

operating time (MD = -1.43 min, P = 0.95), hospital stay (MD = 1.31 days, P = 0.17), and retained stone rate (RR = 1.73, P = 0.38).

Also, a meta-analysis by Alexakis et al,<sup>39</sup> showed that there was no significant differences between the two groups with regard to mortality (OR, 1.2; 95% CI, 0.32–4.52), total morbidity (OR, 0.75; 95% CI, 0.53–1.06), major morbidity (OR, 0.95; 95% CI, 0.60–1.52) and the need for additional procedures (OR, 1.58; 95% CI, 0.76–3.30).

In conclusion; the present meta-analysis showed that both Laparoscopic Cholecystectomy (LC) and Endoscopic Retrograde Cholangiopancreatography (ERCP) in a one-step procedure in comparison to the standard two-step procedure were safe and effective in the management for gallstone disease and biliary duct calculi.

Single stage takes shorter procedural duration, hospital stay, lower cost and lower complication rate in comparison to two stage procedure, however both stage procedures have similar success rates.

Further clinical studies with larger sample size and longer follow-up are needed to confirm our results and to identify risk factors of adverse events.

## Conclusion

The present meta-analysis showed that both Laparoscopic Cholecystectomy combined with Endoscopic Retrograde Cholangiopancreatography (ERCP) in a one-step procedure had the advantages of shorter procedural duration, less hospital stay, lower cost and lower complication rate in comparison to two stage procedure, however both stage procedures have similar success rates. Another advantage of the one-stage procedure is clearing the CBD and removing the gall bladder at the same time so CBD stents would not be required to be inserted and removed in another session later. However, one-stage procedure is not feasible in all hospitals due to required preparations of the Operations Room in contrast to the two-stage procedure.

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