Laparoscopic Excision Versus Open Excision for the Treatment of Choledochal Cysts: A Systematic Review and Meta-Analysis

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In 1723, Vater first described choledochal cyst and in 1977, Todani \textit{et al} classified this disease. For many years, open excision (OP) as the standard procedure made a great impact in the treatment of choledochal cyst. Since 1995, when Farello \textit{et al} first reported laparoscopic choledochal cyst excision, laparoscopic excision (LA) has been used worldwide. However, its safety remains a major concern. The aim of this meta-analysis was to compare OP with LA in treating choledochal cyst and then to determine whether LA is safe and valid. The design of this study involved systematic review and meta-analysis. Data sources were Medline, Ovid, Elsevier, Google Scholar, Embase, and Cochrane library. The study selection entailed comparative cohort studies. For data extraction, 2 investigators independently assessed selected studies and extracted the following information: study characteristics, quality, outcomes data, etc. For the results, 7 comparative cohort studies about the effectiveness of LA compared with OP were performed meta-analysis. The results showed that although the LA group had a longer operative time (MD = 56.57; 95\% CI = 32.20–80.93; \(P < 0.00001\)), LA had a shorter duration of hospital stay (MD = −1.93; 95\% CI = −2.51 to −1.36; \(P < 0.00001\)), and recovery of bowel function (MD = −0.94; 95\% CI = −1.33 to −0.55; \(P < 0.00001\)). Meta-analysis found no significant difference between most of the 2 groups: bile leak (RR = 0.60; 95\% CI = 0.29–1.24; \(P = 0.17\)), abdominal bleeding (RR = 0.33; 95\% CI = 0.01–8.98; \(P = 0.51\)), pancreatitis (RR = 0.26, 95\% CI = 0.06–1.03; \(P = 0.06\)), total postoperative complications (RR = 1.04; 95\% CI = 0.66–1.62; \(P = 0.88\)). The LA group had significant lower rates in intraoperative blood transfusion (RR = 0.20; 95\% CI = 0.11–0.38; \(P < 0.00001\)), and adhesive intestinal obstruction (RR = 0.17, 95\% CI = 0.11–0.38; \(P < 0.00001\)).

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CI = 0.04–0.77; \( P = 0.02 \). In conclusion, compared with open excision, laparoscopic excision is a safe, valid, and feasible alternative to open excision.

Key words: Laparoscopic excision – Open excision – Choledochal cyst – Meta-analysis

In 1723, Vater first described choledochal cyst, a condition in which dilatations occur throughout the biliary tree. Later in 1977, Todani et al classified this disease. It is more common in Asian females, with an incidence of 1 per 1000 in Japan and about 3 to 4 times more likely to occur in females than in males. It is usually a surgical problem of infancy or childhood; however, in approximately 20% of cases, it is recognized in adults. Modern imaging techniques have facilitated the diagnosis of choledochal cyst at any time from antenatal to adult life. Symptoms of choledochal cyst include abdominal pain, jaundice, cholangitis, and may eventually lead to malignant transformations, so early diagnosis and proper surgical excision are very important. For many years, open excision, as the standard procedure, made great impact in the treatment of choledochal cyst. Since the first report about laparoscopic choledochal cyst excision by Farello et al in 1995, laparoscopic excision (LA) has been used worldwide. Undoubtedly, LA has many advantages, including excellent visualization, less pain, and fewer scars. However, its safety remains a major concern. So far, there have been many studies published comparing the safety of laparoscopic excision (LA) versus open operation (OP) in the treatment of choledochal cyst. We pooled these studies and performed this systematic review and meta-analysis to determine whether LA is safe and valid compared with OP.

Materials and Methods

Search strategy

The aim of this systematic review and meta-analysis was to include all publicly available data for comparing the safety and valid of laparoscopic excision and open excision on choledochal cyst. We systematically searched Medline, Ovid, Elsevier, Google Scholar, Embase, and the Cochrane Library for studies published between 1995 and 2014, with the search terms "choledochal cyst," "biliary dilatation," "bile duct cyst," "laparoscopic excision," "open excision," and combinations of these 4 terms. Authors of the original studies were contacted for more detail if needed.

Study selection criteria

Before reviewing specific reports, we defined criteria for the inclusion of studies. To enter the analysis, studies had to meet the following criteria: (1) report the 2 surgical techniques for the treatment of choledochal cyst; (2) compare the 2 surgical techniques; (3) include at least one of the outcome measures, mentioned below, used for analysis; (4) be published as a full paper; and (5) be a comparative cohort study.

Exclusion criteria

The exclusion criteria are the following: (1) review articles; (2) meeting abstracts; (3) studies that only include 1 surgical technique; (4) studies with no comparative data; (5) full text not in English or insufficient information available in English abstract; and (6) if a study in 1 report overlapped with another report. We give up the study that is in smaller scale.

Quality assessment and data extraction

We adopted the Newcastle–Ottawa Scale (NOS), designed specifically for observational studies to assess the quality of selected studies. NOS focuses on 3 separate sections of a case control or cohort study, and the number of stars represents the assessment score. The maximal score of NOS is 9 stars: 4 stars for the selection process, 2 stars for comparability, and 3 stars for exposure/outcome. Two investigators independently assessed selected studies and extracted the following information: first author, year of publication, study type, mean age, number of population, and main outcomes of interest (operative time, hospital stay, intraoperative blood transfusion, bile leak, pancreatitis, postoperative complications in total, etc.). The reviews reached consensus at each of the screening processes.

Statistical analysis

Statistical analysis was conducted using Review Manager 5.1 (Cochrane Collaboration). Relative risk (RR) and mean difference (MD) with 95% confidence interval (CI) were used as the measurement of dichotomous and continuous variables, respectively.
According to methods introduced by Hozo et al.\textsuperscript{12} and the Cochrane Handbook for Systematic Reviews of Interventions, medians with ranges were converted into means with standard deviations. RR represented the odds of an adverse event occurring in the LA group compared with the OP group. A value of RR of less than 1 indicated a beneficial outcome favoring the LA group. \( P \) values <0.05 indicated statistical significance. Heterogeneity was quantified by the \( I^2 \) statistic. A study with an \( I^2 \) less than 50\% was considered to have no evidence of heterogeneity, and then the fixed-effects model was applied to pool the results; otherwise, the random-effects model was used.

Results

Characteristics of included studies

The study screening process is shown in Fig. 1, through which, in total, 1408 patients (611 in the LA group, 797 in the OH group) from 7 studies were enrolled.\textsuperscript{13–19} All 7 studies were not randomized controlled trials, but instead observational studies published between 2007 and 2012. The characteristics of these 7 studies are listed in Table 1. (Supplementary data are available online.)

The scale of the studies ranged from 16 to 616 (mean, 201), and age of patients ranged from 7 days to 18 years. No statistical difference was detected in scale and age of studies between the LA group and OP group.

Postoperative complications morbidity and functional outcomes were the primary parameters for the comparison between LA and OP. The main data for meta-analysis are summarized below and in Table 2.

When selected studies were assessed by the Newcastle-Ottawa scale, most studies showed a medium risk for selection bias, low to medium risk for comparability, and high risk for outcome (Table 3).

### Table 1 Characteristics of 7 studies in the meta-analysis

| Author, year | Study type | Number of patients | Age (Mean ± SD) | Operative time (Mean ± SD, min) | Hospital stay (Mean ± SD, day) |
|--------------|------------|-------------------|----------------|--------------------------------|--------------------------------|
| Aspelund, 2007 | R          | LA: 4             | 230 ± 182 w    | 392 ± 40                       | 9.5 ± 5.8                      |
|               |            | OP: 12            | 234 ± 286 w    | 281 ± 63                       | 6.8 ± 3.0                      |
| She, 2009     | R          | LA: 10            | 45 m           | NC                             | NC                             |
|               |            | OP: 65            |                |                                |                                |
| Liem, 2011    | R          | LA: 309           | 48.7 ± 2.3 m   | 182.5 ± 22.2                   | 7.0 ± 0.2                      |
|               |            | OP: 307           | 63.5 ± 2.9 m   | 147.1 ± 6.33                   | 9.1 ± 0.2                      |
| Diao, 2011    | R          | LA: 216           | 4.2 y (7 d–18 y)| NC                            | 7.41 ± 2.39; 9.94 ± 3.47       |
|               |            | OP: 200           | 4.6 y (13 d–17 y)|                          |                                |
| Liuming, 2011 | R          | LA: 39            | 5 y (3 m–13 y) | 241 ± 52(185–450)              | 5.5 ± 0.9(4–10)                |
|               |            | OP: 38            | 4 y(2 m–15 y)  | 190 ± 31(135–270)              | 7.0 ± 1.4(5–12)                |
| Cherqaoui, 2012| R          | LA: 9             | 53.2(0.4–156) m| 288 ± 86.7                     | 12.67 ± 8.26                   |
|               |            | OP: 10            | 62.5(12–192) m | 206 ± 34.8                     | 7.9 ± 2.378                    |
| Wang, 2012    | R          | LA: 22            | NC             | NC                             | NC                             |
|               |            | OP: 165           |                |                                |                                |

\( R \), retrospective study; \( w \), week; \( m \), month; \( y \), year; \( NC \), not clear.
Results of meta-analysis

Operative time
Four trials (Aspelund, 2007; Liem, 2011; Liuming, 2011; & Cherqaoui, 2012) contributed data (Table 1), including a total of 728 patients (361 in LA, 367 in OP). All studies showed the duration of operation was longer in the laparoscopic group than in the open group. The analysis found statistically significant heterogeneity ($P < 0.01$), which was high ($I^2 = 76\%$), then a random-effect model was adopted. Pooled mean difference (MD = 56.57; 95% CI = 32.20–80.93; $P < 0.00001$) indicated that the difference is statistically significant (Fig. 2).

Hospital stay
Five trials (Aspelund, 2007; Liem, 2011; Diao, 2011; Liuming, 2011; and Cherqaoui, 2012) reported the time of hospital stay (Table 1), including a total of 1146 patients (579 in LA, 567 in OP). In 2 trials, the times of hospital stay were significantly higher in the LA group, while the OP group showed higher times in the other 3 studies. The analysis found statistically significant heterogeneity ($P < 0.01$), which was high ($I^2 = 73\%$), then a random-effect model was adopted. Pooled mean difference (MD = 1.93; 95% CI = 2.51 to 1.36; $P < 0.00001$) stated statistically shorter time in the LA group (Fig. 3).

Recovery of bowel function
Five studies (Aspelund, 2007; Liem, 2011; Diao, 2011; Liuming, 2011; Cherqaoui, 2012) involved time of recovery of bowel function (Table 2), including a total of 1146 patients (579 in LA, 567 in OP). One study reported the time in OP group was shorter, 3 studies reported the time in the LA group was shorter; meanwhile for the rest, 1 study reported the time was

Table 2  Main outcomes of LA and OP

| Study          | Number of patients | Intraoperative blood transfusion | Return of bowel function (Mean ± SD.day) | Bile leak | Abdominal bleeding | Anastomotic stenosis | Pancreatitis | Adhesive intestinal obstruction | Postive operation complications in total |
|----------------|--------------------|----------------------------------|------------------------------------------|-----------|-------------------|----------------------|--------------|---------------------------------|------------------------------------------|
| Aspelund (2007)| LA: 4              | NC                               | 3.8 ± 1.3                                | NC        | NC                | NC                   | NC           | NC                              | 2                                        |
|                | OP: 12             |                                  | 3.8 ± 1.0                                |           |                   |                      |              |                                 | 3                                        |
| She (2009)     | LA: 10             | NC                               | NC                                       | 0         | 1                 | 1                    | 0            | 0                               | 2                                        |
|                | OP: 65             |                                  | 0                                         | 1         | 1                 | 1                    | 1            | 0                               | 10                                       |
| Liem (2011)    | LA: 309            | 10                               | 2.5 ± 0.1                                | 7         | 1                 | 0                    | NC           | NC                              | 12                                       |
|                | OP: 307            | 34                               | 3.7 ± 0.1                                | 6         | 5                 | 12                   |              |                                 | 17                                       |
| Diao (2011)    | LA: 216            | 0                                | 3.05 ± 1.43                              | 2         | 2                 | 0                    | 0            | 0                               | 8                                        |
|                | OP: 200            | 16                               | 4.06 ± 2.34                              | 11        | 5                 | 3                    | 5            | 8                               |                                          |
| Liuming (2011) | LA: 39             | 0                                | 3.5 ± 0.7 (3–6)                          | 1         | NC                | NC                   | 0            | 0                               | 8                                        |
|                | OP: 38             | 3                                | 4.9 ± 0.9 (3–7)                          | 1         |                   |                      | 1            | 1                               | 6                                        |
| Cherqaoui (2012)| LA: 9             | NC                               | 3.33 ± 1.5                               | 1         | NC                | NC                   | 0            | NC                              | 1                                        |
|                | OP: 10             |                                  | 2.5 ± 0.71                               | 0         |                   |                      | 1            | 1                               |                                          |
| Wang (2012)    | LA: 22             | NC                               | NC                                       | NC        | NC                | NC                   | NC           | NC                              | 3                                        |
|                | OP: 165            |                                  |                                           |           |                   |                      |              |                                 | 14                                       |

Table 3  Quality assessment of included studies using the NOS

| Study          | Selection | Comparatorability | Outcome |
|----------------|-----------|-------------------|---------|
|                | Star      | Risk of bias      | Star    | Risk of bias | Star | Risk of bias |
| Aspelund, 2007 | ★★★      | high              | ★★      | medium       | ★   | high         |
| She, 2009      | ★★★★★    | medium            | ★★★★★  | low          | ★   | high         |
| Liem, 2011     | ★★★★★    | medium            | ★★★★★  | low          | ★   | high         |
| Diao, 2011     | ★★★★★    | medium            | ★★★★★  | low          | ★☆☆☆ | low         |
| Liuming, 2011  | ★★★★★    | medium            | ★★★★★  | medium       | ★   | high         |
| Cherqaoui, 2012| ★★★★★    | medium            | ★★★★★  | medium       | ★   | high         |
| Wang, 2012     | ★★★★★    | medium            | ★★★★★  | high         | ★   | high         |

Stars identify high quality choices. A maximum of one star for each high quality choice item within the Selection and Exposure/Outcome categories; maximum of two stars for Comparability.
equal between the 2 groups. The analysis found statistically significant heterogeneity \((P < 0.01)\), which was high \((I^2 = 73\%)\), then a random-effect model was adopted. Pooled mean difference \((MD: -0.94; 95\% CI: -1.33 to -0.55; P < 0.00001)\) indicated statistically shorter time in the LA group (Fig. 4).

### Intraoperative blood transfusion

Three studies (Liem, 2011; Diao, 2011; Liuiming, 2011) compared the rates of intraoperative blood transfusion with 1111 patients (566 in LA group, 545 in OP group; Table 2). All 3 studies showed a higher rate of intraoperative blood transfusion in the OP group. Pooled RR \((RR = 0.20; 95\% CI = 0.11–0.38; P < 0.00001)\) showed statistical difference of intraoperative blood transfusion between the 2 groups. Heterogeneity was not significant \((P = 0.21, I^2 = 36\%\); Fig. 5).

### Bile leak

Four studies (Liem, 2011; Diao, 2011; Liuiming, 2011; Cherqauoui, 2012) compared the incidences of bile leak with 1130 patients (575 in LA group, 555 in OP group; Table 2). Pooled RR \((RR = 0.60; 95\% CI = 0.29–1.24; P = 0.17)\) showed no significant difference between the 2 groups. Heterogeneity was not significant \((P = 0.14, I^2 = 45\%\); Fig. 6).

### Abdominal bleeding

Three studies (She, 2009; Liem, 2011; Diao, 2011) contributed data, including 1109 patients (537 in LA group, 572 in OP group; Table 2). Heterogeneity was high \((I^2 = 66\%, P = 0.05)\), so a random-effect model was adopted. Meta-analysis \((RR = 0.79; 95\% CI = 0.09–7.15; P = 0.85)\) showed no increase in relative risk for the occurrence of abdominal bleeding in LA group compared with the OP group (Fig. 7).

### Anastomotic stenosis

Three studies (She, 2009; Liem, 2011; Diao, 2011) compared the incidences of anastomotic stenosis, including 1109 patients (537 in LA group, 572 in OP group; Table 2). A random-effect model was

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**Table 1:** Pooled Estimates of Operative Time

| Study or Subgroup | Laparoscopic excision | Open excision | Mean Difference | Mean Difference |
|-------------------|-----------------------|--------------|----------------|----------------|
|                    | Mean | SD | Total | Mean | SD | Total | Weight | FC Random | 95% CI | Year |
| August, 2007      | 4.8 | 0.9 | 44 | 7.3 | 1.2 | 44 | 34 | 2.8 | 0.018 | 0.18 | 3.007 |
| Liem, 2011        | 4.0 | 0.5 | 35 | 4.9 | 0.7 | 35 | 30 | 2.5 | 0.015 | 0.11 | 0.79 |
| Diao, 2011        | 3.9 | 0.5 | 34 | 4.6 | 0.7 | 34 | 26 | 2.0 | 0.010 | 0.05 | 0.26 |
| Total (95% CI)    | 3.7 | 0.6 | 133 | 4.8 | 0.9 | 133 | 104 | 2.4 | 0.009 | 0.14 | 3.29 |
adopted, as heterogeneity was statistically significant \((P = 0.02, \, \, \, I^2 = 75\%)\). Pooled RR \((RR = 0.33, \, \, \, 95\% \, CI = 0.01–8.98; \, \, \, P = 0.51)\) showed no significant difference between the 2 groups (Fig. 8).

### Pancreatitis

Four studies (She, 2009; Diao, 2011; Liuming, 2011; Cherqaoui, 2012) compared the rates of pancreatitis, including a total of 589 patients (276 in LA group; 313 in OP group; Table 2). There was no pancreatitis occurred in the LA group, while 8 incidences of pancreatitis occurred in the OP group. When meta-analysis was performed, no statistically significant difference \((RR = 0.26, \, \, \, 95\% \, CI = 0.06–1.03; \, \, \, P = 0.06)\) was found. Evidence of significant heterogeneity was lacking \((P = 0.51, \, \, \, I^2 = 0; \, \, \, \text{Fig. 9})\).

### Adhesive intestinal obstruction

Three studies (She, 2009; Diao, 2011; Liuming, 2011) contributed data, including a total of 570 patients (267 in LA group; 303 in OP group; Table 2). The meta-analysis showed a lower rate of adhesive intestinal obstruction in the LA group. \((RR = 0.17, \, \, \, 95\% \, CI = 0.04–0.77 ; \, \, \, P = 0.02)\). Heterogeneity was not significant \((P = 0.21, \, \, \, I^2 = 37\%; \, \, \, \text{Fig. 10})\).

### Total postoperative complications

Six studies (Aspelund 2007; She, 2009; Liem, 2011; Liuming, 2011; Cherqaoui, 2012; Wang, 2012) contributed data, including 990 patients (393 in the LA group, 597 in the OP group; Table 2). In total postoperative complications, the outcome of meta-analysis \((RR = 1.04 ; \, \, \, 95\% \, CI = 0.66–1.62 ; \, \, \, P = 0.88)\) showed no statistical difference between the LA and OP groups. Heterogeneity was not significant \((P = 0.72, \, \, \, I^2 = 0\%; \, \, \, \text{Fig. 11})\).

### Discussion

This study is the first systematic and meta-analysis comparing LA with OP in the treatment of choledochal cyst. The results of the meta-analysis suggested that compared with OP, LA is safe and valid with a shorter...
time of recovery for bowel function and hospital stay, but the operative time of LA is longer. Regarding the most postoperative complications, our meta-analysis found no significant difference, except a statistical lower rate of adhesive intestinal obstruction in the LA group. Beyond that, for the LA group, it was observed that there was notably less need for transfusion, which might be attributed to improved accuracy provided with the magnified view in laparoscopy. The shorter interval for recovery of bowel function and hospital stay postoperatively may indicate a quicker recovery in the LA group than the OP group.

Since Farello et al first reported laparoscopic excision of choledochal cyst in 1995, several authors have reportedly used this technique for surgical resection of choledochal cysts, and many comparative studies about LA and OP have been performed in different medical centers. Most studies implied that laparoscopic excision was a safe and feasible alternative to open excision in the treatment of choledochal cysts, which was also supported by our meta-analysis.

Although operative time was statistically longer in LA than OP (Fig. 2), it seemed to make little difference. There is no doubt that the laparoscopic approach requires more instruments and is technically more demanding. Meanwhile, along with the wide use of laparoscopic excision in clinical surgery and the increase of surgeons’ experience, the operation time for laparoscopic procedure might be shortened and approach that needed for an open procedure.

The main limitation of this meta-analysis is the lack of randomized controlled trials. Although most of the comparative cohort studies seem to be robust, risk of selection bias still existed; it was the surgeons’ preference and experience that determined the allocation of patients to either the LA or OP groups. As heterogeneity was high and the scale of some studies was small, caution should be applied in the generalization and interpretation of our meta-analysis.

Conclusion

Although we lack sufficient randomized controlled trials, the present meta-analysis study remains the best evidence for outcomes. Based on the present evidence, we make a cautious conclusion that, compared with open excision, laparoscopic excision is safe and valid. These findings warrant further investigation.

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