



Laparoscopic versus open appendectomy in pediatric patients with complicated appendicitis: a meta-analysis

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Abstract

Background Acute appendicitis is a common condition in the pediatric population. In patients with uncomplicated appendicitis, laparoscopic appendectomy (LA) is preferred as compared to open appendectomy (OA). However, in patients with complicated appendicitis (CA), as defined as suppurative, gangrenous or perforated appendicitis, or appendicitis with periappendicular abscess formation, the decision to perform OA or LA remains unclear.

Methods The PRISMA guidelines were adhered to. An electronic database search from 1997 to 2017 was performed using the Cochrane, Medline, PubMed, Scopus, Ovid, Embase, and Web of Knowledge databases. Data analysis, including subgroup analysis of randomized-control trials, was performed using RevMan 5.3. Assessment of methodological and statistical heterogeneity, as well as publication bias of the included studies, was performed.

Results Six randomized-control trials (296 LA versus 373 OA) and 33 case-control trials (3106 LA versus 4149 OA) were analyzed. Compared to OA, LA has a shorter length of stay (WMD = -0.96, 95% CI -1.47 to -0.45) and a lower rate of surgical site infection (OR 0.37, 95% CI 0.25–0.54), although the rates of intraabdominal abscess formation were similar (OR 1.01, 95% CI 0.71–1.43). LA was also shown to have lower readmission rates, lower incidences of postoperative ileus or intestinal obstruction, lower incidence of reoperation, as well as a shorter time taken to oral intake. Operative time for OA was shorter than LA (WMD = 12.44, 95% CI 2.00–22.87).

Conclusion While studies in the past have associated LA with higher rates of intraabdominal abscess in patients with CA, our meta-analysis has shown that they were similar. Considering this, together with other improved postoperative outcomes, LA should be the procedure of choice in pediatric patients presenting with CA.

Keywords Complicated appendicitis · Laparoscopic appendectomy · Open appendectomy · Intraabdominal abscess

Acute appendicitis (AA) is a common condition requiring surgical intervention in the pediatric population, with an incidence rate of 9.4 cases per 10,000 person-years [1]. Due to increasing usage of specific diagnostic techniques

such as Computed Tomography (CT), there is an increasing trend in the annual rate of AA [2]. Complicated appendicitis (CA), defined as histologically or intraoperatively diagnosed gangrenous appendicitis (GA), perforated appendicitis (PA), suppurative appendicitis (SA), and appendicitis with an abscess or periappendicular mass, represents 28% of all cases [2]. Both the historical and recent epidemiological data have also shown that among all age groups, AA occurs most frequently in pediatric patients [2, 3] while CA has a positive correlation with younger age groups [4].

Before 1983—the year which the first laparoscopic appendectomy (LA) was reported by Semm [5], surgical treatment for AA solely comprised open appendectomy (OA) that was initially described by McBurney in 1894 [6]. In the last 20 years, LA is increasingly adopted over OA due to multiple benefits associated with minimally invasive surgery, such as lower rate of surgical site infection (SSI),

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reduced incidence of postoperative ileus, shorter length of hospital stay (LOS), and earlier return to regular activity [7–9]. Thus, for patients with simple, uncomplicated AA, several meta-analyses have shown that LA is the procedure of choice [9–14].

On the other hand, CA is associated with poorer outcomes such as higher rates of postoperative SSI and intraabdominal abscess (IAA) formation, leading to more frequent readmissions and delayed return to normal activities [15–17]. Several studies have also found that LA is associated with a significantly higher rate of IAA [10, 11, 18–21], and therefore, OA was deemed as the gold standard for patients with CA [18].

More than two decades after LA was first described, this meta-analysis aims to review the current literature and compare the associations of LA and OA concerning various postoperative outcomes to determine which approach is more suitable in pediatric patients with CA.

Materials and methods

Search and selection strategy

An electronic database search in the period of 1997 to 2017 was independently performed by 2 authors between October and November 2017 using the Cochrane Library, Medline, PubMed, Scopus, Ovid, Embase, and Web of Knowledge databases. Using Boolean operators ‘AND’ and ‘OR,’ we used all possible combinations of the Mesh terms: ‘child, children, pediatric, paediatric, appendectomy, appendectomy, laparoscopy, laparoscopic, endoscopy, endoscopic, minimally invasive, open, and conventional.’ The electronic search was supplemented by a hand-search of published abstracts from 2002 to 2017 from the International Pediatric Endosurgery Group (IPEG), European Association for Endoscopic Surgery (EAS), the American College of Surgeons (ACS), and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). Back-referencing was used to identify potential studies and relevant citations to be included in our analysis. A flow diagram that illustrates the literature search is shown in Fig. 1. The full search strategy carried out in PubMed (Supplementary Table 1) is included in the supplementary material.

Eligibility

Studies were included if they (1) studied pediatric patients with CA; (2) defined CA similar to ours; (3) performed a comparison between LA and OA; (4) reported on at least one of the 9 outcomes that we are interested in studying. Our primary objectives are IAA, SSI, LOS, and operating time (OT). Our secondary outcomes are postoperative

ileus/intestinal obstruction (IO), the time taken to oral intake (TTOI), need for percutaneous intervention, need for reoperation, and rate of readmission. In this analysis, IAA is defined as an abscess involving the organ or space that was found on direct examination during the operation, or by radiological imaging [22].

Publications were excluded if they (1) were not written in English; (2) included data based on other criteria besides pediatric patients; (3) used data from large administrative databases; (4) contained duplicated or incomplete data; (5) combined data for uncomplicated appendicitis with CA; (6) did not compare the outcomes of LA and OA; (7) were not either Case Controlled Trials (CCTs) or prospective studies. As no specific definition for ‘pediatric patients’ was set, no publications were excluded based on the age range of their participants.

All abstracts were screened by the 2 authors and selected full-text articles were reviewed to determine their eligibility for inclusion in this pooled analysis. Any disagreements regarding the inclusion or exclusion of a study were resolved by discussing with a third author. For publications that required payment to access its full-text article, we contacted the corresponding author to obtain access. Where we did not get a reply, we extracted data from the abstract.

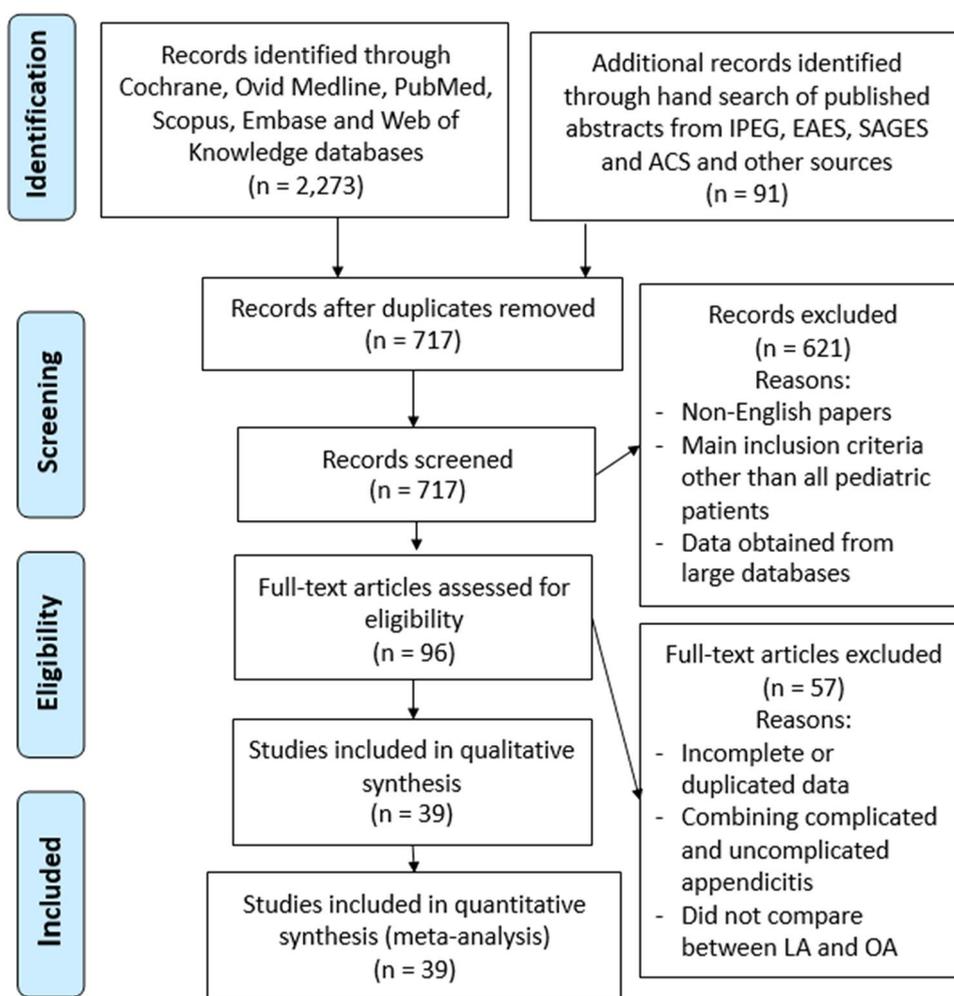
Data extraction and validity assessment

This study was undertaken according to the Cochrane Handbook for Systematic Reviews of Interventions [23] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Two authors independently extracted data from included studies and recorded them in a pre-designed and piloted data abstraction form to the reduce risk of error (Supplementary Tables 2 and 3). Any disagreement was resolved by discussing with a third author.

Data analysis

The meta-analysis was performed using the RevMan 5.3 from the Cochrane Collaboration. A pre-requisite for inclusion of a dichotomous outcome in this meta-analysis was the report of sufficient data to form 2 by 2 contingency tables. Thus, in cases where the incidence of a particular outcome is 0 for both LA and OA, respectively, no data were entered. Furthermore, as many of the papers did not report the number of conversions from LA to OA, the data for OA were analyzed with an as-treated protocol. For continuous outcomes to be included in this meta-analysis, studies had to report mean values and standard deviations. When mean and range were provided, but not standard deviation, standard deviation estimates were calculated using the ‘Finding SDs’ tool recommended by the Cochrane Collaboration (<http://training.cochrane.org/resource/revman-calculator>). On the

Fig. 1 Flow diagram of our search and selection strategy in accordance with the PRISMA statement



other hand, when both mean and standard deviation are unavailable and instead median and range were provided, conversion to mean and standard deviation estimates were performed using an online calculator (http://vassarstats.net/median_range.html) which derived its methods devised by Hozo et al. [24].

For dichotomous data, such as rates of SSI and IAA, the Mantel–Haenszel statistical method and odds ratios (OR) with 95% Confidence Intervals (CI) was employed. For continuous data, such as OT, LOS, and TTOI, the weighted mean difference (WMD) with 95% CI was calculated. The WMDs and ORs were both considered to be statistically significant when the P value was 0.05 and below. If WMD is negative or OR is less than one, LA is favored, and the point estimate is considered to be statistically significant if the diamond, representing the summary of WMD or OR from the pooled studies with 95% confidence intervals, does not cross the line of no effect.

Assessment of risk of bias and methodological heterogeneity was carried out using the Methodological index for non-randomized studies (MINORS) for CCTs [25]

(Supplementary Table 4) and the Cochrane Risk of Bias Tool for Randomized Controlled Trials (RCTs) [26] (Supplementary Table 5). Statistical heterogeneity of the included studies was determined using the χ^2 and I^2 statistical tests, while publication bias was assessed using funnel plots. A random effects model was employed due to a high level of heterogeneity between studies, as well as the presence of multiple factors contributing to clinical heterogeneity, such as sample size and the year of publication.

Results

6 RCTs (296 LA versus 373 OA) and 33 CCTs (3106 LA versus 4149 OA) were included in the analysis.

Study characteristics

The characteristics of the included studies are summarized in Supplementary Table 1. Although we included studies that were published within the last 20 years, 26 out of 39

studies were relatively new and published in the last decade. All participants identified through this meta-analysis were below 20 years of age. The maximum age defined by most papers is between 15 and 18 years. A lower limit was not defined by most studies, with a minority using 1–2 years of age as the minimum to be included. The majority of studies included PA or GA in their definition of CA, with or without the presence of peritonitis. Baseline demographics of included participants were reported and compared in most of the studies. Between the OA and LA groups, the baseline demographics were comparable except in 6 studies, which reported statistically significant differences in variables such as age, weight, gender, and histopathological subtype of appendicitis. Common exclusion criteria include incidental or interval appendectomies; presence of an appendicular mass and/or an abscess; administration of intravenous (IV) antibiotics for a prolonged period of time; and past medical or surgical history that may complicate the surgery and confound the outcomes, such as previous major abdominal operation, immunosuppressive disorders, bleeding diathesis, kidney or liver dysfunction, and neurological disorders. However, not all studies employed the same exclusion criteria, contributing to a certain degree of clinical and methodological heterogeneity. We also identified other factors in the study demographics that may account for clinical heterogeneity, such as the duration over which the outcomes were measured; the country where the study took place; the size of study; and the demographics of the patients.

The characteristics of the interventions of included studies are summarized in Supplementary Table 2. The specialty and level of experience of performing surgeons and their numbers varied widely between papers and were commonly underreported. However, the operative techniques employed in both LA and OA did not differ widely between studies. In almost all studies, LA was performed with 3 trocars, while OA was done with an incision in the right iliac fossa (RIF). Only an exception of 3 studies reported using other surgical incisions such as midline, paramedian, and pararectal incision. In LA, mesoappendix division was carried out using either electrocautery or ultrasonic dissector in most of the studies, with a few studies utilizing clip ligation. Endoloop was commonly used for securing of the appendicular base, with some using an extracorporeal knot, intracorporeal suture ligation, endoscopic stapler, and biological clips. However, retrieval of the appendix was underreported and inconsistent, with half using a retrieval bag and another half through the trocar. Similarly, the usage of drains in LA and OA was mixed and reported only by several studies. Intra-peritoneal lavage was done with normal saline and, occasionally, antibiotics containing solution. Concerning perioperative management, the type, duration, timing, and route of antibiotic regime given varied widely between studies. Postoperative IV or oral triple antibiotic therapy, consisting

of ampicillin or cephalosporin, aminoglycoside, and metronidazole, is most commonly prescribed, but this is not consistent between all studies.

Methodological quality

The methodological quality and risk of bias assessment of the studies are shown in Supplementary Tables 3 and 4, respectively. The risk of bias within the studies ranged from intermediate to high among studies. This was mainly because of factors such as the absence of observer blinding and statistical power calculations in RCTs, inadequate reporting or statistical testing of significant independent variables that may have influenced the outcomes, and insufficient reporting of perioperative care and its standardization, all potentially influencing internal and external validity.

Diagnosis of CA, surgical techniques, and antibiotic prescribing were quite homogenous, with reasonable validity, and thus a decision was made to proceed with a meta-analysis of outcomes.

Stratification analysis during the meta-analysis did not reveal any differences between the various groups analyzed, apart from the analysis comparing the RCT against the CCT groups where on some occasions, the former subgroup found no difference in some outcomes between LA and OA. This difference can potentially be attributed to the small number of patients included in the RCTs compared to the CCTs.

Primary outcomes

Intraabdominal abscess

31 studies (3 RCTs [27–29] and 28 CCTs [30–52]) reported the incidence of IAA that occurred in the LA and OA groups, respectively (Fig. 2). The incidence of IAA occurring in LA was 7.93% (224 out of 2826 cases) and in OA was 8.14% (317 out of 3894 cases). Our meta-analysis showed that there is no statistically significant difference between both groups (OR 1.01, 95% CI 0.71–1.43) in the combined analysis of RCTs and CCTs. Similarly, in the subgroup analysis of RCTs, LA was comparable to OA with respect to the rates of IAA (OR 0.82, 95% CI 0.11–6.19). There is high risk of statistical heterogeneity for the combined analysis ($I^2 = 56%$, $P < 0.0001$) and for the RCT subgroup analysis ($I^2 = 88%$, $P = 0.0003$).

Surgical site infection

31 studies (5 RCTs [27–29, 53] and 26 CCTs [8, 30–37, 39–52]) reported the number of SSI that occurred in the LA and OA groups, respectively (Fig. 3). The incidence of SSI occurring in LA was 5.91% (163 out of 2,757 cases) and in OA was 12.3% (467 out of 3802 cases). Our meta-analysis

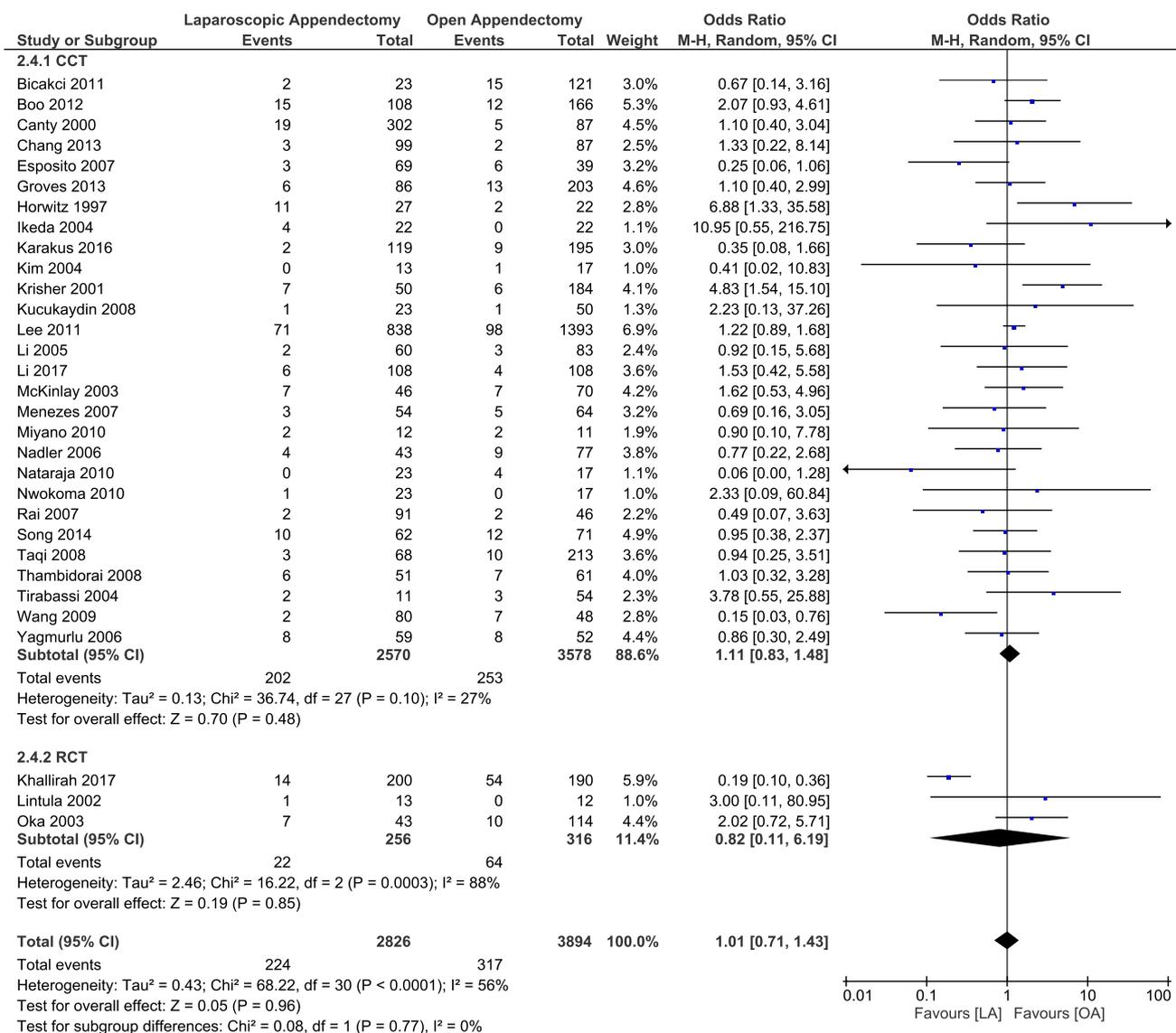


Fig. 2 Forest plot of IAA in the meta-analysis of LA versus OA

showed that LA has statistically significant lower rates of SSI as compared to OA (OR 0.37, 95% CI 0.25–0.54), with a moderate risk of statistical heterogeneity (I² = 52%, P = 0.0004). Subgroup analysis of the 5 RCTs also demonstrated LA has statistically significant lower rates of SSI (OR 0.62, 95% CI 0.41–0.95) with no risk of statistical heterogeneity (I² = 0%, P = 0.63).

Length of stay

19 studies (2 RCTs [28, 54] and 17 CCTs [16, 30, 32–34, 37, 38, 40, 42, 44–46, 48–52]) reported the LOS for the LA and OA groups, respectively (Fig. 4). The combined analysis of all 19 studies showed that there is a statistically significant shorter LOS for LA (WMD = -0.96 days, 95% CI -1.47 to

-0.45) with a high risk of statistical heterogeneity (I² = 91%, P < 0.00001). In the subgroup analysis of RCTs, there is no statistically significant difference between both groups (WMD = 0.77 days, 95% CI -0.26–1.79) with no risk of statistical heterogeneity (I² = 0%, P = 0.51).

Operating time

16 studies (2 RCTs [28] and 14 CCTs [8, 16, 30, 33, 34, 37, 40, 42, 44–46, 48, 51, 52]) reported the operating time for the LA and OA groups, respectively (Fig. 5). In the combined analysis of RCTs and CCTs, OA has a significantly shorter OT (WMD = 12.44 min, 95% CI 2.00–22.87) with a high risk of statistical heterogeneity (I² = 94%, P < 0.00001). In the 2 RCTs [28] which reported data for OT, OA was

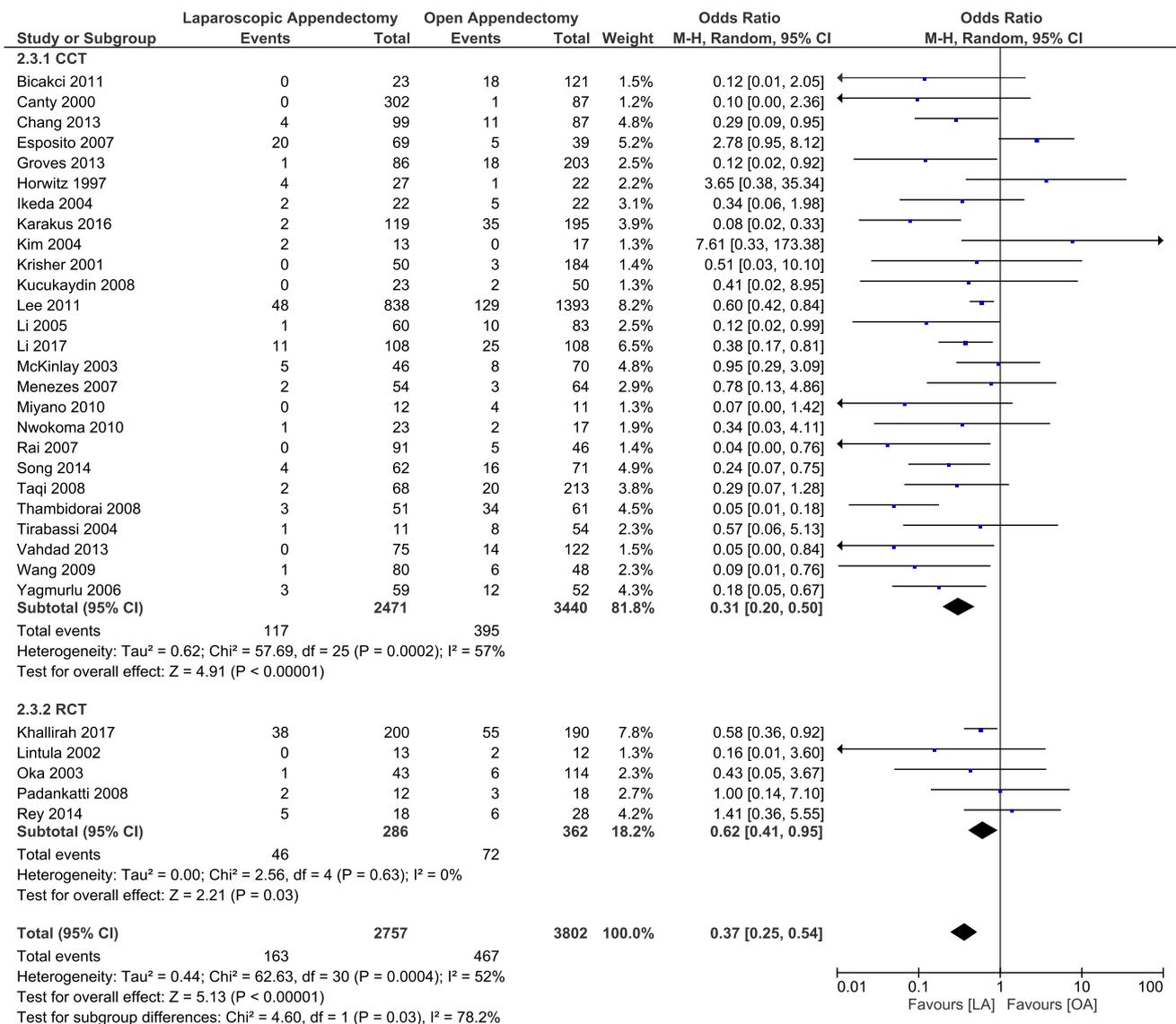


Fig. 3 Forest plot of SSI in the meta-analysis of LA versus OA

also shown to have a shorter OT (WMD = 29.48 min, 95% CI 17.88–41.08) with no statistical heterogeneity ($I^2 = 0\%$, $P = 0.67$).

Secondary outcomes

Postoperative ileus or intestinal obstruction

24 studies (3 RCTs [29, 53] and 21 CCTs [8, 16, 30, 33, 35–40, 43, 45–49, 52, 55–57]) reported the rates of postoperative ileus or IO for the LA and OA groups, respectively (Supplementary Fig. 6). The incidence of postoperative ileus or IO occurring in LA was 3.50% (60 out of 1,713 cases) and in OA was 7.32% (131 out of 1789 cases). The combined analysis of CCTs and RCTs showed that there is a

statistically significant lower rate of postoperative ileus/IO for LA (OR 0.56, 95% CI 0.36–0.87) with no statistically significant heterogeneity ($I^2 = 20\%$, $P = 0.19$). On the other hand, the subgroup analysis of RCTs did not show a statistically significant difference between both groups (OR 0.52, 95% CI 0.13–2.06) with no risk of statistical heterogeneity ($I^2 = 0\%$, $P = 0.94$).

Readmission

12 studies (2 RCTs [27, 29] and 10 CCTs [8, 16, 32, 33, 38, 39, 41, 50, 56]) reported the readmission rates for the LA and OA groups, respectively (Supplementary Fig. 7). The incidence of readmission required in LA was 6.74% (111 out of 1,646 cases) and in OA was 9.32% (254 out of 2726

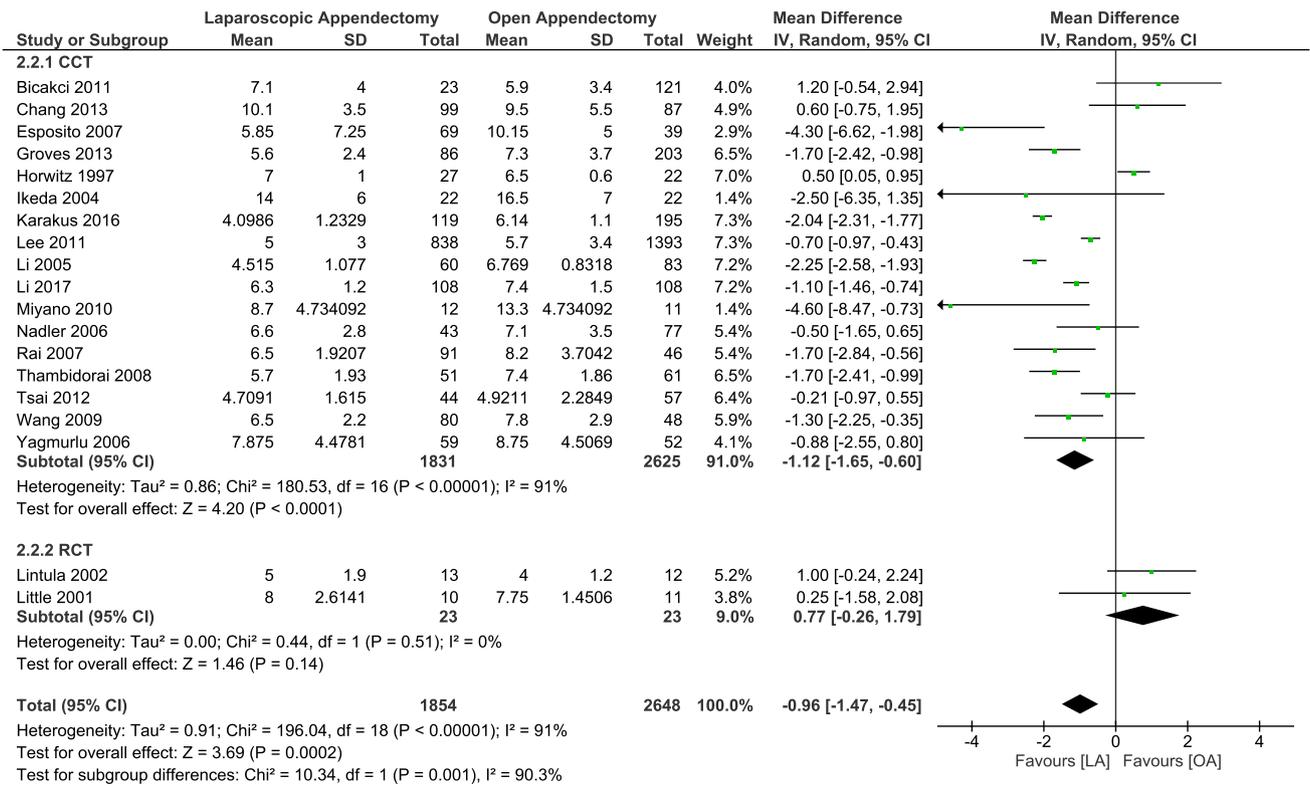


Fig. 4 Forest plot of LOS in the meta-analysis of LA versus OA

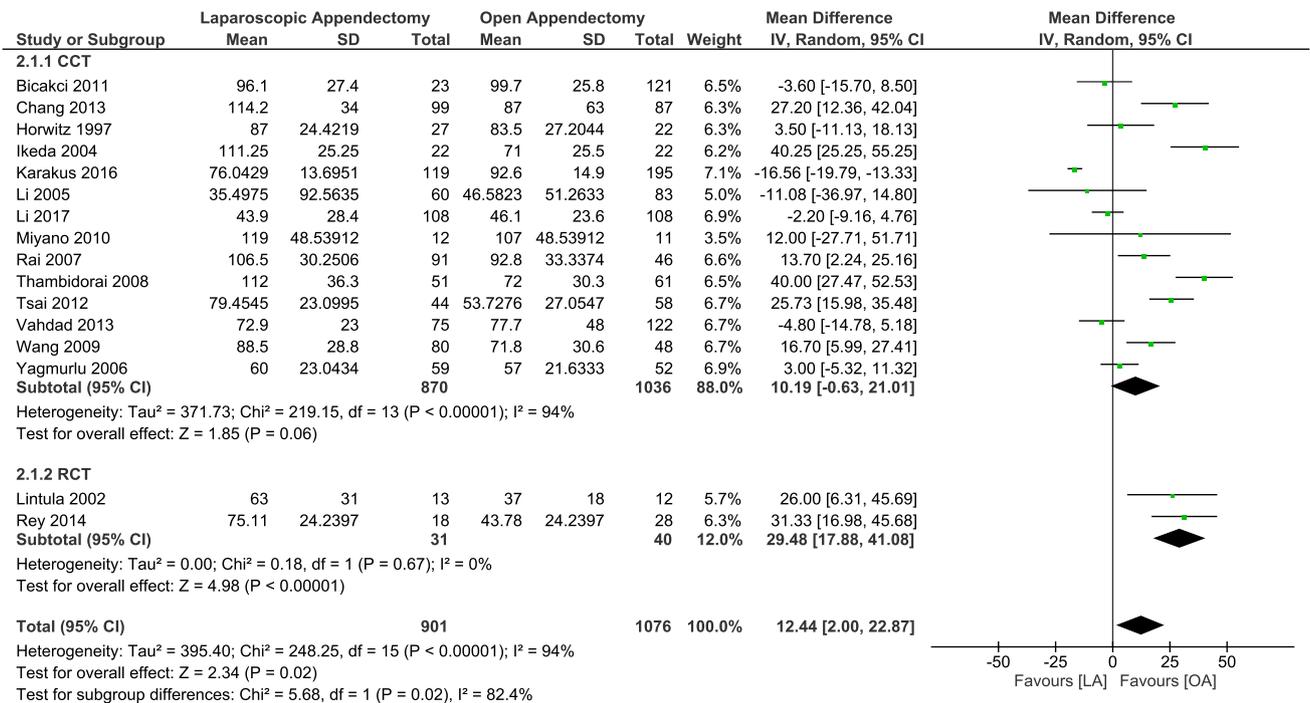


Fig. 5 Forest plot of OT in the meta-analysis of LA versus OA

cases). The combined analysis of the 12 studies showed that there is no statistically significant differences in the rate of readmission (OR 0.77, 95% CI 0.42–1.40) with a moderate risk of statistical heterogeneity ($I^2 = 69\%$, $P = 0.0002$). Similarly, in the subgroup analysis of RCTs, there is a statistically lower rate of readmission for LA as compared to OA (OR 0.27, 95% CI 0.07–1.00) with a moderate risk of statistical heterogeneity ($I^2 = 40\%$, $P = 0.20$).

Need for reoperation

13 studies (2 RCTs [53] and 11 CCTs [8, 30, 38–40, 45, 46, 49, 50, 56, 57]) reported the number of reoperations that occurred in the LA and OA groups, respectively (Supplementary Fig. 8). The incidence of reoperations occurring in LA was 2.70% (22 out of 814 cases) and in OA was 7.57% (89 out of 1,175 cases). Our meta-analysis showed that LA resulted in a statistically significant reduced incidence of reoperation as compared to OA (OR 0.43, 95% CI 0.23–0.78), with low risk of statistical heterogeneity ($I^2 = 22\%$, $P = 0.22$). However, the 2 RCTs [53] did not show any statistically significant difference between LA and OA (OR 0.19, 95% CI 0.02–1.71) with no risk of statistical heterogeneity ($I^2 = 0\%$, $P = 0.47$).

Need for percutaneous intervention

9 studies (1 RCT [27] and 8 CCTs [32, 35, 40, 41, 43, 45, 48, 56]) reported the number of percutaneous interventions performed postoperatively in the LA and OA groups, respectively (Supplementary Fig. 9). The incidence of percutaneous interventions occurring in LA was 6.82% (97 out of 1422 cases) and in OA was 8.11% (176 out of 2170 cases). Our meta-analysis showed that there was no statistically significant difference between both groups (OR 1.23, 95% CI 0.92–1.65), with moderate risk of statistical heterogeneity ($I^2 = 76\%$, $P < 0.0001$). On the other hand, the RCT [27] demonstrated statistically lower rate of percutaneous intervention needed in LA (OR 0.19, 95% CI 0.10–0.36) with no risk of statistical heterogeneity.

Time taken to oral intake

5 studies (1 RCT [54] and 4 CCTs [37, 40, 44, 45]) reported the TTOI for the LA and OA groups, respectively (Supplementary Fig. 10). Our meta-analysis showed that the LA group has a statistically shorter TTOI as compared to OA (WMD = -0.88 days, 95% CI -1.09 to -0.66), with no statistical heterogeneity ($I^2 = 0\%$, $P = 0.57$). On the other hand, the RCT [54] did not show any statistically significant difference between the 2 groups (WMD = -0.50 days, 95% CI -1.78 to 0.78) with no risk of statistical heterogeneity.

Publication bias

A funnel plot is plotted for IAA (Supplementary Fig. 11) and SSI (Supplementary Fig. 12) to assess the publication bias of each outcome. The funnel plots are symmetrical and suggest that there is minimal publication bias for studies included in the analyses of IAA and SSI.

Discussion

In pediatric patients with CA, the decision to perform LA has been controversial due to the challenging nature of performing minimally invasive surgery in an area of distorted anatomy and severe inflammation. Dissecting and visualizing the appendix clearly, performing and determining the adequacy of peritoneal lavage, and preventing the spread of infection from the inflamed appendix to its surrounding abdominal organs are demanding, especially if a laparoscopic approach is adopted [15–17]. Some authors have reported a higher incidence of postoperative IAA in patients with CA who had undergone an appendectomy laparoscopically, and hence do not advocate LA in pediatric patients with CA [52]. Others have also proposed that LA has to be exercised with caution, especially for cases associated with an appendicular mass, due to the risk of bleeding and visceral injury [58]. Furthermore, performing LA may necessitate conversion to OA in cases with severe inflammation or adhesions [48]. On the other hand, LA has been shown to be technically easy to perform with good postoperative outcomes in pediatric patients with uncomplicated appendicitis [11]. In recent years, as laparoscopic surgery becomes more mainstream and widely practiced, various authors have then published and reported favorable outcomes when LA is utilized in the setting of CA [11, 59].

Our meta-analysis provides an updated comparison and uses the largest number of subjects (7924 participants from prospective, retrospective, and RCT publications) as compared to other older reviews on the same topic. The findings have shown that LA is favored for most of the primary and secondary outcomes, namely SSI, LOS, postoperative ileus or IO, the rate of reoperation, and TTOI. Additionally, when we looked at the rates of IAA, there was no significant difference between both groups.

Similar to the findings of earlier reviews performed in both children and adults, we found that LA is associated with a much lower incidence of SSI (5.91 vs. 12.3%, $P < 0.00001$) [11, 59]. These results are also consistent with studies done with substantial administrative and clinical databases of both age groups [60–63]. Subgroup analysis conducted with 4 RCTs also demonstrated a statistically significant difference favoring LA (16.1 vs. 19.95, $P = 0.03$). Multifactorial reasons for this have been cited in our included studies, such as

usage of an endoscopic bag in LA which reduces the contact between the infected appendix and surgical site, as well as a smaller wound size created in LA as compared to OA [33, 42, 48]. Furthermore, surgeons using laparoscopy may have better visualization of and access to the entire abdominal cavity, helping them to achieve a more thorough aspiration of the infected fluid [64].

Additionally, LA also confers a shorter LOS (WMD = -0.96 days, $P=0.0002$), lower rates of postoperative ileus or IO (3.50 vs. 7.32%, $P=0.01$), lower likelihood of reoperation (2.70% vs. 7.57%, $P=0.006$), and a shorter TTOI (WMD = -0.88 days, $P<0.00001$). Like SSI, these findings are consistent with what previous studies have shown in both adult and children [10, 11, 59]. Lower incidence of postoperative ileus or IO in LA could be explained by various mechanisms, such as minimal trauma to the abdominal wall and peritoneal cavity; lower likelihood of introducing foreign bodies; better hemostasis; and quicker return of bowel motility [55]. Patients undergoing LA may also have earlier mobilization, owing to the improved postoperative outcomes mentioned throughout this “Discussion” section. They also help to account for a shorter LOS that is associated with LA. Even though the subgroup analysis conducted with only RCTs does not show any significant differences for these outcomes, it is noteworthy that a small number of RCTs and sample size is analyzed in the subgroups, respectively.

Furthermore, our meta-analysis is the first to show that there is no significant difference in the rates of IAA between LA and OA. Three meta-analyses were, respectively, published in 2012, 2013, and 2017 on CA but found that LA is associated with higher rates of IAA [11, 21, 65]. This observation could be accounted for by possible spread of infection during pneumoperitoneum; inadequate peritoneal lavage; incomplete removal of the appendix; and aggressive manipulation of the inflamed appendix. However, as the uptake of LA increased over the years, so did the experience and skills of surgeons in laparoscopy [49, 53]. During this time, LA techniques were possibly standardized and improved as well, resulting in the reduction of complications such as IAA [35]. These advancements are also evident from the decreasing trend of conversion from LA to OA [36, 59]. A prospective way to observe this correlation between gain in experience and outcomes has been proposed by Canty et al., by following the vertical development of 4 very experienced surgeons as they switched from 1 technique to another [47]. A comparison of the outcomes between the first 10-year period (1997–2007) and the second 10-year period (2008–2017) could also be valuable evidence to substantiate the learning curve of laparoscopic techniques over the past few decades.

Aside from the aforementioned surgeon factors, LA also contains inherent technical advantages over OA. For example, LA allows the surgeon to visualize better and access

all parts of the peritoneal cavity, enabling easier detection, effective drainage, and irrigation of localized collections during surgery. This also makes LA a suitable intervention for obese children as the abdomen may be more easily manipulated. Additionally, the difference in results observed in this meta-analysis as compared to others on the same topic may be contributed by the difference in methodology. Besides being more updated, the search strategy, which includes not only online databases but also conference abstracts, is more thorough. As a result, this meta-analysis also provides the largest number of participants studied on this topic.

Of all the outcomes, only the length of operation is favored when OA is performed (WMD = 12.44 min, $P=0.02$). As compared to simple, uncomplicated appendicitis, locating and removing the appendix, as well as achieving a thorough washout can be very time consuming, leading to a significantly longer OT. In addition to this, performing LA also involves more instruments and, thus, requires a more elaborate setup than OA. However, there is a decreasing trend in the differences in OT due to improvements in laparoscopy, such as hemostatic devices that help to achieve quicker dissection [19]. Besides, with better visualization afforded with LA, we may expect a decreasing trend in OT as laparoscopy allows the appendix to be easily found, manipulated, and removed quickly [47]. Ultimately, LOS is a more critical factor than OT due to multiple benefits for the patients such as earlier return to school, better psychological outcomes for the child, lower healthcare costs, and less disruption to daily activities and organization of the whole family.

Our findings corroborate with the most updated meta-analysis on the adults with CA, published 1 year ahead of our paper by Athanasiou et al. [59]. For example, both papers demonstrated that the rate of IAA is comparable between LA and OA. They have also shown, similar to our findings, that LA is associated with a significantly lower rate of SSI, reduced LOS, shorter TTOI, and longer OT when compared to OA.

It is important to note that limitations exist in our meta-analysis and thus, to a lesser degree, heterogeneity within our included studies and between the existing meta-analyses could account for some of the novel results presented in this analysis. While our findings are the first to prove that there are no significant differences in IAA between both groups, factors such as the experience of the surgeon; the severity of inflammation; the degree of intraperitoneal contamination; time to diagnosis; and time to surgery could confound the results. Despite the influence of such confounding factors, they were underreported in most studies and would be difficult to correct. Furthermore, selection bias may exist when the surgeon chooses the procedure as this is primarily based on the surgeon's preference and patient factors. For example,

bigger-sized children with a fat-laden peritoneum may more likely undergo LA, contributing to the higher incidence of IAA in LA in previous meta-analyses. Besides, the definition of outcomes, how they are measured and the duration over which they were observed were underreported. Despite this, the 3 existing meta-analyses based on the same topic and age group [11, 21, 65] have substantiated other parts of our analysis, including a reduced rate of SSI associated with LA. We also acknowledge that there exists heterogeneity due to differences in the treatment protocols and inclusion criteria between our included studies. Finally, the allocation and assessment of outcomes were not blinded, and this may be understandable because to do so will be extremely difficult and almost impossible.

Conclusion

In the past, LA was avoided in pediatric patients with CA for fear of higher rates of IAA postoperatively [28, 47, 52]. This was supported by findings in earlier meta-analyses [11, 21, 65]. Our meta-analysis, aimed at providing an updated comparison and the strengths of LA and OA, respectively, has shown that both groups are associated with comparable rates of IAA, making it a safe and feasible intervention. Furthermore, LA is associated with better postoperative outcomes, importantly a lower rate of SSI and a shorter LOS. In addition to the previous meta-analyses, the rate of reoperation and the rate of postoperative percutaneous intervention have been included in our analysis. Lastly, to substantiate the learning curve of laparoscopic techniques over the years, future work still needs to be done to compare the outcomes between the first and second decade of our study.

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Compliance with Ethical Standards

Disclosures Zhi Xuan Low, Glenn Kunnath Bonney, Jimmy Bok Yan So, Dale Lincoln Loh, and Jun Jie Ng have no conflicts of interest.

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