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Review Article

To close or not to close? A systematic review and meta-analysis of wound closure in appendicectomy

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ABSTRACT

Background/objective: Published studies have shown conflicting results regarding the rate of wound infection between primary and delayed closures in open appendicectomy. This meta-analysis was performed with the aim to summarize all available evidence.
Methods: A literature search was carried out using Medline, PubMed, EMBASE and Cochrane databases from inception to January 2018. Randomized controlled studies that compared primary closure (PC) to delayed closure (DC) in appendicectomy were included. Pooled odds ratio and 95% confidence interval were calculated using Mantel-Haenszel fixed-effects model when there was no heterogeneity identified.
Results: Of the 471 retrieved studies, eight met the eligibility criteria and were included in the analysis. These trials included 1,263 patients, of whom 623 patients underwent delayed closure and 640 primary closure. Surgical Site Infections SSI rates were not significantly different between the DC and PC groups (16.25% & 12.68% respectively. OR=0.60, 95% CI: 0.23-1.54. There was a high heterogeneity among the analyzed studies (I^2=82%).
Conclusion: This meta-analysis found no benefit in performing delayed primary closure over primary closure in open appendicectomy.

1. Introduction

Appendicitis represents the most common surgical emergency in the world [1]. Every year around 300,000 people are admitted in the US with appendicitis [2]. Approximately 8% of the Western population will develop appendicitis during their life, with a peak incidence between 10 and 30 years of age [3].

Surgical site infection (SSI) is one of the most common causes of morbidity following any procedure, this risk is greater in contaminated surgeries [4–6]. In complicated appendicitis, the SSI rate can range from 9% to 53% [7]. SSIs increase post-operative pain, hospital stay, and cost [8].

Delayed primary closure of appendicectomy wounds has been one of the interventions aimed at reducing SSI since the time of First World War [9]. This was believed to increase blood supply and oxygen in the wound [10]. The 'dirty' wound is left open after a procedure, with the plan for a delayed closure (DC), hence providing the wound a few days to turn 'clean' [11].

However, this approach has not universally found acceptance. Many prefer to perform a primary closure (PC) instead [12,13]. The opponents challenge this approach as it unnecessarily increases length of hospital stay and cost of treatment [14].

There have been several studies [15,16] and randomized controlled trials (RCTs) [4,5,17–22] in the past which have attempted to answer this question, albeit with mixed results.

As one would expect, this dilemma is less frequent nowadays in the era of laparoscopic appendicectomy. However, in many parts of the world open appendicectomy is still the standard practice. In fact, even in the UK and Europe, one third of appendicetomies are still performed utilizing the open approach [23].

The aim of this meta-analysis is to compare SSIs in primary and delayed closures in appendicectomy through a right lower quadrant incision.

2. Materials and methods

This meta-analysis was undertaken and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [24].

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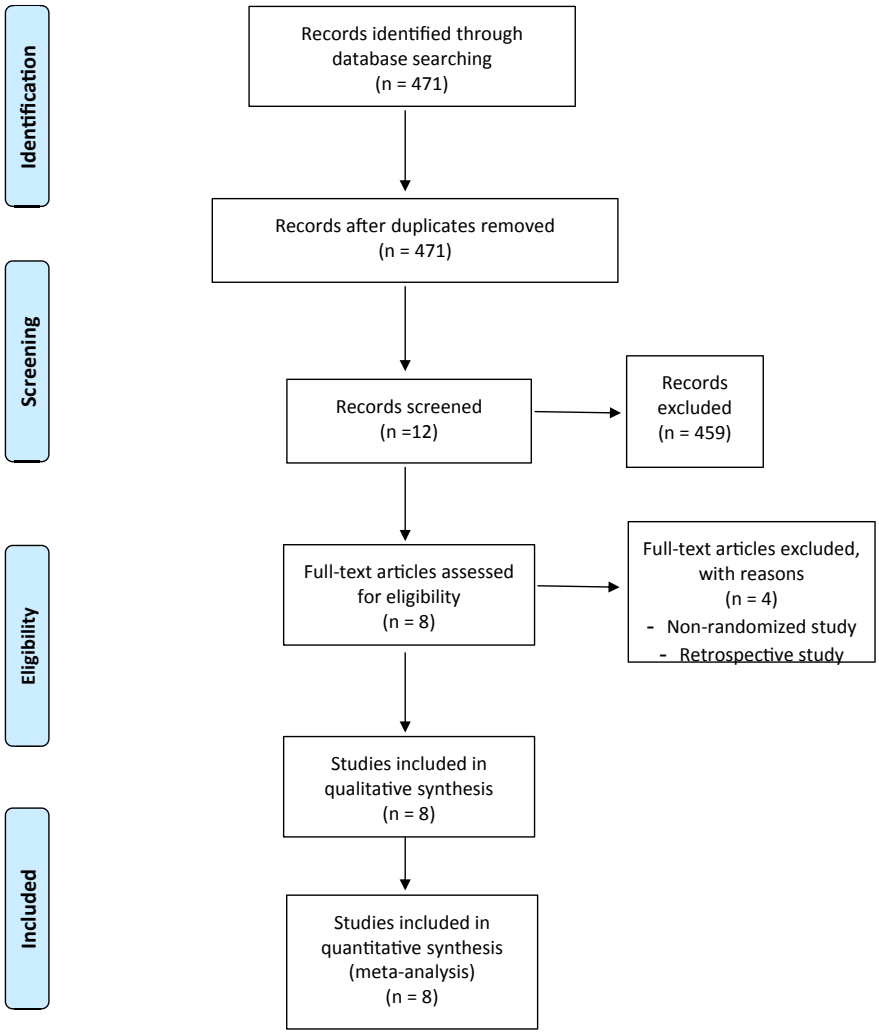

Fig. 1. PRISMA diagram showing flow of citations through systematic review process.

Table 1
Characteristics of included study.

Study (year)	n	Age group	PC SSI %	DC SSI %	PC technique	DC technique & final closure	Examination/follow-up	Recommendations
Pettigrew (1981) [4]	122	Adults	36.6	54.7	Interrupted nylon monofilament	Gauze dressing, closure on day 5	At 4 weeks	PC
Tsang (1992) [20]	63	Children	21.1	24	Interrupted nylon	Saline dressing changed daily, skin tapes on day 4	Till satisfactory wound healing	PC
Cohn (2001) [5]	17	Adults	50	0	Skin staples, subcutaneous not closed	Saline-soaked gauze, evaluated day 3, final closure with adhesive strips	Daily until discharge, then after 1 week and 1 month	DC
McGreal (2002) [22]	174	Adults & children	5.6	11.6	Subcuticular braided 4/ 0 polyglycolate	Ribbon gauze soaked in 1% povidone-iodine inserted between interrupted nylon sutures, wick soaked daily and then removed on day 4	Daily during hospital stay and at 4 weeks (clinical/ telephone)	PC
Khan (2012) [19]	100	Adults	10	8	NA	Daily dressing, closure after 3 −5 days or after infection settled	Stitches removed on day 7	PC
Chiang (2012) [21]	70	Adults & children	38.9	2.9	Monofilament nylon	0.5% Betadiene-soaked gauze, daily change, closure on day 5 if wound clean	Observed for at least 2 weeks	DC
Ahmad (2014) [18]	158	Adults	39.2	6.3	Subcuticular or interrupted Prolene 2/0	Saline dressing, closure on day 4,	Followed up till day 8, skin stitches removed day 10	DC
Siribumru-ngwong (2017) [17]	598	Adults	7.3	10	Nonabsorbable monofilament suture or staple	Twice daily saline-soaked gauze, closure on day 3–7 with same suture as PC	Before discharge, at 1 week and at 1 month (clinical/ telephone)	PC

PC – primary closure, DC – delayed primary closure, SSI – surgical site infection, NA – not applicable.

2.1. Outcomes of interest

The primary outcome was to assess the rates of surgical site infections among patients undergoing open appendicectomies via a right lower quadrant incision followed by PC or DC.

2.2. Eligibility criteria

The following inclusion criteria were applied: Clinical prospective Randomized Controlled Trials (RCTs) comparing PC with DC in open surgery for appendicitis. Outcomes assessed in the studies included: 'surgical site infection' or 'wound infection'. Only publications in English language were included. There were no restrictions on dates published.

2.3. Search strategy

A systematic literature search was performed of Medline, PubMed, EMBASE and Cochrane databases. All published studies in English up to January 2018 were assessed. Hand-searching of the literature references was also used during the same period. The following search terms were used; [title/abstract]: "appendicitis" OR "complicated appendicitis" OR "perforated appendicitis" OR "gangrenous appendicitis" AND "delayed primary closure" OR "delayed closure" OR "primary closure" OR "wound infection" OR "surgical site infection". Abstracts were screened for relevance.

2.4. Study selection

The studies were extracted independently by PA and KH according to the eligibility criteria. Any discrepancies were resolved by consensus discussion with OA. The following data were extracted: publication year and type (i.e., abstract or full article), study location, number of patients and demographics, technical considerations in wound closure for PC and DC, method and frequency of evaluation for infection, wound infection rate, follow-up and secondary outcomes assessed in each study.

2.5. Data collection & analysis

Data was extracted from the identified publications and recorded in Review Manager Version 5.3 (RevMan 5.3, The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). Odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated from the total number of patients and the number of events within each group. The wound infection rate in each group (PC vs DC) was the primary endpoint.

The meta-analysis was performed using RevMan 5.3. Pooled odds ratios of SSI were calculated. Mantel-Haenszel random effects model was used. Heterogeneity was assessed using χ^2 and I^2 tests (significant heterogeneity if $p < 0.1$ or $I^2 > 50\%$). Significance of the overall effect was determined using the z test. P values ≤ 0.05 were considered statistically significant.

2.6. Assessment of bias

The selected studies were assessed independently by PA and KH for bias using the Cochrane Collaboration's tool for the assessment of bias [25]. Areas of disagreement were resolved by consensus discussion with OA.

Publication bias was assessed visually using a funnel plot of the reviewed studies.

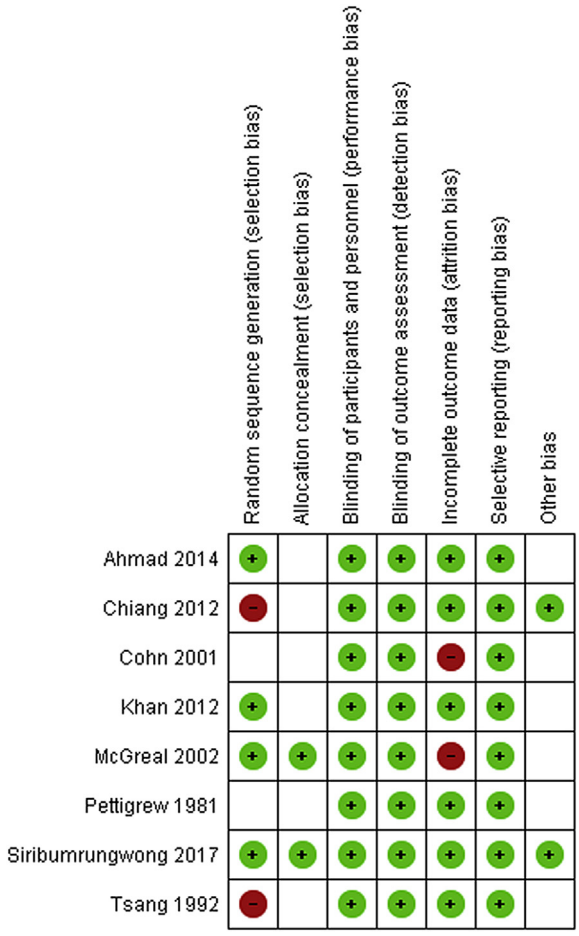

Fig. 2. Assessment of bias for each included study in seven domains according to the Cochrane Collaboration's tool. (+) = low risk of bias; (−) = high risk of bias; (empty) = uncertain risk of bias.

3. Results

The search resulted in 471 studies. After screening titles and abstracts, 12 papers were selected for full-text review. After applying the eligibility criteria, eight of these studies were included in the meta-analysis [4,5,17–22]. The PRISMA flow diagram is shown in Fig. 1. All of the selected studies were full text articles. Table 1 shows the characteristics of the included studies.

1263 patients were included in this meta-analysis, including 623 patients in the DC group and 640 patients in the PC group. The main characteristics of each study are shown in Table 1. The assessment of bias is depicted in Fig. 2.

3.1. Surgical site infection

Surgical site infection was considered the primary outcome in this meta-analysis. Eight RCTs assessed SSI [4,5,17–22]. These trials included 1263 patients, of whom 623 patients underwent delayed closure and 640 primary closure. 183 patients had positive events (SSIs), including 79 patients (12.68%) in the DC group and 104 patients (16.25%) in the PC group. There was no significant difference between the groups (OR = 0.60, 95% CI: 0.23–1.54, p = 0.29) (Fig. 3). There was a significant heterogeneity ($P < 0.00001$; $I^2 = 82\%$).

The funnel plot for SSIs was asymmetric, indicating the presence of publication bias (Fig. 4).

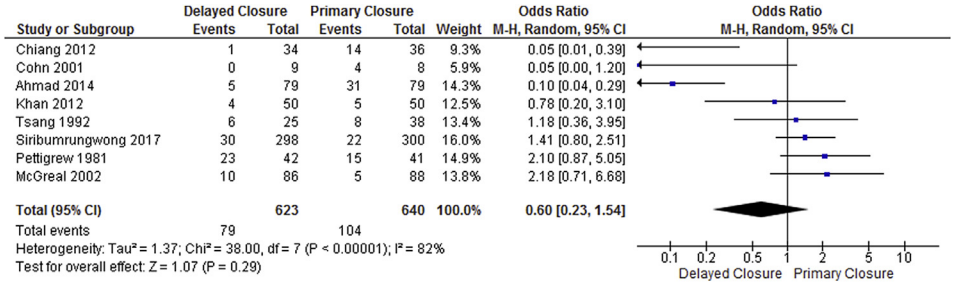

Fig. 3. Forest plot of SSI rates in DC and PC.

4. Discussion

Appendicectomy is one of the most common operations in the United Kingdom and USA [3,26]. Therefore, any improvement in the current standard of care can potentially have a significant impact on a large population, and could have positive effects in cost-efficacy.

A recent multicenter prospective observational cohort study carried out in centers in UK, Spain, Japan, Hong-Kong, Australia and New Zealand showed that initial laparoscopic approach was performed in 66.3% of patients and 6.9% of patients had to been converted to an open procedure [23]. Thus, over 40% patients had wound closures performed for right lower quadrant incisions. This finding makes this meta-analysis relevant even in the laparoscopic era in managing acute appendicitis. Additionally, in many parts of the world, the open surgical approach to manage acute appendicitis is still the standard of treatment due to lack of laparoscopic equipment and expertise.

This study analyzed 1263 patients. Pooled data showed no statistically significant difference between the groups. Eight studies evaluated SSI rate between study groups [4,5,17–22]. There was no benefit in DC in terms of improvements in SSI rate with an overall odds ratio of 0.60 (CI 0.23–1.54, p = 0.29).

Some of the reviewed studies assessed secondary outcomes, such as length of hospital stay [19], and cost analysis [17]. Both studies showed advantageous effect of PC over DC. However, the lack of sufficient data to pool and interpret the results make it hard to interpret these secondary outcomes. Therefore, they were not included in this review.

There have been previous attempts to answer our study question. Ruckinski et al. [27] conducted a review of over 2500 patients with complicated appendicitis from 27 studies. However, that review included non-controlled and retrospective studies. Henry et al. [11] published a systematic review and meta-analysis, but their study was focused mainly on the pediatric population and included 347 patients only. Siribumrungwong et al., more recently [7], and Bhangu et al. [28] conducted 2 similar meta-analyses on contaminated abdominal wounds, and even though studies of open appendectomies were considered, other operations varied from laparotomies to ileostomy closures. Thus to our knowledge this is the only meta-analysis specifically asking the question of wound infections in open appendectomies exclusively, and including children and adult age groups.

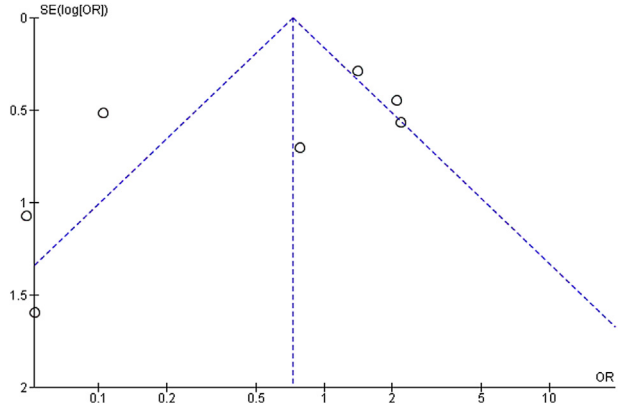

Fig. 4. Funnel plot analysis of publication bias. The outcome was Surgical site infection rate.

There are several limitations in this meta-analysis. The most striking perhaps being the significant heterogeneity, which was more than 80% (Fig. 3). This may be a result of inconsistency in the use of dressing and antibiotics in the groups. Nevertheless, when the one obvious outlier study (Ahmad et al. [18]) was eliminated from the analysis, the heterogeneity went down to 65%, and still the OR showed no significant change to favor either of the groups (OR = 0.94, 95% CI: 0.44, 2.00, p = 0.86) in terms of SSI. This substantial heterogeneity could be due to the fact that this outlier study used a high effect size (15%) compared to the other reviewed studies, which had an average effect size of 8%.

Another limitation was the detection of publication bias as shown in Fig. 4. This may relate to inclusion of only studies published in English language.

In conclusion, this meta-analysis showed that DC offers no benefit over PC with regard to wound infection following open appendicectomy.

Ethical approval

NA.

Funding

NA.

Author contribution

PA and KH collected and analysed the data. OA helped in analysis and writing up the manuscript.

Conflict of interest statement

NA.

Guarantor

OA.

Research Registration Number

481.

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