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Review Article

Simple ligation versus stump inversion in open appendicectomy: a systematic review and meta-analysis

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ABSTRACT

To perform a systematic review and meta-analysis on post-operative complications after surgery for appendicitis comparing simple ligation with inversion of the appendix stump. PubMed, Medline and Embase databases were searched to identify studies comparing post-operative outcomes in appendicectomy following simple ligation and inversion of the appendix stump. A meta-analysis with a random-effects model was used to calculate pooled odds ratios (OR) and confidence intervals (CI) for each outcome measure of interest. A total of 14 studies were included for meta-analysis, comprising a total of 4037 patients who underwent appendicectomy. There was an increased risk of small bowel obstruction following appendix stump inversion (OR = 4.18, CI = 1.31 – 13.41; p = 0.02; 9 studies). After excluding studies without antibiotic prophylaxis there was no difference between inversion or ligation of the appendix stump with respect to either total infective complications (OR = 1.03; 95% CI= 0.75 – 1.43, 10 studies) or surgical site infection (OR = 1.07; CI = 0.78 – 1.47; 10 studies). Inversion of the appendix stump during appendicectomy may increase risk post-operative small bowel obstruction whilst offering no reduction in post-operative infective complications.

Keywords: Appendicectomy, Stump ligation

INTRODUCTION

Acute appendicitis remains the most common acute surgical condition of the abdomen. Thus, appendicectomy is one of the most commonly performed operations in general surgery.[1] The introduction of laparoscopic appendicectomy (LA) and meta-analyses demonstrating reduced post-operative pain and a shorter hospital stay after LA has led rising popularity of performing appendicectomy via a laparoscopic approach.[2] However, open appendicectomy is still frequently performed with 34% of appendicitis in the UK receiving this procedure. An open approach may be necessary in cases where laparoscopy is contraindicated and following conversion due technical difficulties in the safe excision of the appendix.

Open appendicectomy can be classified as a total or sub-total appendicectomy.[3] A total appendicectomy involves complete removal of the appendix from the caecum, leaving no remnant stump. It is performed to avoid possible stump related complications, for example: abscess of the stump, haemorrhage or stumpitis.[4-6]

The standard operative approach in the United Kingdom is to perform a subtotal appendicectomy where the proximal segment of the appendix is left behind as a stump, which may either be left alone or inverted into the caecum. There are theoretical advantages to inversion of

the appendix stump such as double closure of the caecal wall, reducing contamination from an intra-peritoneal stump and reducing the risk of post-operative adhesions by minimizing the area of exposed enteric surface during the healing period. In contrast, authors have suggested that in practice there is an increased incidence of adhesions with stump inversion, whilst concerns over misdiagnosis of an inverted stump as a caecal neoplasm and the potential for intramural caecal abscess persist.[7,8]

In laparoscopic appendicectomy the stump is not routinely invaginated and in many studies simple ligation has been found to be safe.[9] The purpose of this systematic review and meta-analysis is to comprehensively investigate the post-operative complications following surgery for appendicitis comparing simple ligation with inversion of the appendix stump after open appendicectomy.

METHODS

Search strategy

PRISMA statement guidelines were followed for conducting and reporting meta-analysis data. We searched Medline and Embase from inception to October 2015 using the following search terms "Appendix" OR "Appendicitis" OR "Appendiceal" OR "Appendicectomy" OR "Appendectomy" AND "Invaginate" OR "Invagination" OR "Invert" OR "Bury" OR "Inversion" AND "Stump". The identical terms were used again in PubMed. The search encompassed titles, abstracts, subject headings and registry words. Articles were limited to those published in the English language, animal studies and duplicates were removed.

Study selection

Studies identified from the differing searches were merged and titles and abstracts were examined to incorporate relevant material only. Full text versions were obtained of eligible articles and were reviewed by authors (VC and PW) separately prior to inclusion. Disagreements between authors were resolved through joint discussion of the particular manuscript. Studies were only included in the meta-analysis where comparative data between inversion and ligation of the appendix stump was presented. Outcome measures assessed were post-operative small bowel obstruction, surgical site infection, total infective complications and formation of pelvic abscess. Studies involving children, case reports and letters were excluded. Studies that did not overtly report outcome measures or where outcomes could not be derived were not included.

Data extraction

Data extraction was performed by authors into a Microsoft Excel spreadsheet (MS Office 2010). Relevant data included study author, date range, study type, patient demographics, outcome measures, length of stay, operative time, use of antibiotics and exclusion criteria for complicated appendicitis. The total infective complication rate, defined as superficial and intra-abdominal sepsis incidence, was evaluated. Length of stay, re-operative and fistulae rates were noted if reported.

Risk of bias

Study quality was assessed using the Newcastle-Ottawa score for case-control studies in meta-analysis. 9 stars is the maximum value attainable. Publication bias was assessed by funnel plot for each outcome measure. To reduce bias, analysis was repeated without outlier studies.

Statistical analysis

Statistical analyses were performed on Rev Man 5.3 (http://tech.cochrane.org/revman; 2014) and SPSS (version 20; IBM). Patient group characteristics were evaluated using $\chi 2$ test without Yates correction and unpaired t-test for dichotomous and continuous variables respectively. A p value of <0.05 was considered statistically significant. Outcome measures for meta-analysis were chosen to test the null hypothesis of equivalent post-operative complications in both groups. Primary outcome measures comprised of total infectious complications, wound infections, post-operative bowel obstruction and pelvic abscess formation.

Dichotomous variables were analysed with the Mantel-Haenszel method and random-effects model. This model was preferred as it does not presume homogeneity between included studies in terms of methodology or clinical characteristics and thus allowing a more moderate analysis than the fixed effects model. Certain outcome measures were not stated by all studies, therefore the total number of patients in simple ligation and stump inversion was variable. No outcome measures were expressed as continuous variables. Odds ratio, 95% confidence interval, Forest and funnel plots were generated by Rev Man software for each outcome.

Outcomes

The meta-analysis outcomes were chosen to test the null hypothesis of equivalent results with and without stump inversion after open appendicectomy. Primary outcome measures were: wound infection, small bowel obstruction, pelvic abscess and total abdominal sepsis complications.

RESULTS

The search strategy identified a total of 79 articles from Medline, Embase and PubMed databases (following English language and human filters). Duplicates excluded 43 records. This left 36 full-text articles to be assessed for eligibility. A further 22 were excluded (2 letters, 5 case

reports and 3 studies involving children). Following full-text review 14 studies were included for meta-analysis. (Figure 1 and Table 1).

Table 1: Characteristics and results of included studies.

						Demographics				Group equivalence		Totals		
						Age		Sex (M-F)			Bias	n		
Author	Country	Design	NOS	Dates	FUP	Inverted	Ligated	Inverted	Ligated	Exclude perforated appendicitis	Prophylactic antibiotics	Total n	Inverted n	Ligated n
Watters	Scotland	PR	7	1979 - 1980		21.7 (6-46)	18.1 (5-43)	29-30	21-23	Yes	no	103	59	44
Sinha	Scotland	R	6	1970-1974		NS	NS	NS	NS	Yes	no	643	210	433
Engstrom	Sweden	PR	7	1977-1982		29 (14-85)	29 (15-91)	187-187	196-165	No but derivable	variable	735	374	361
Misgar	India	RC	6	1995-1997		NS	NS	NS	NS	No	NS	100	50	50
lavonius	Finland	RC	6	1996		35 (16-81)	35 (16-78)	53-47	63-37	No, but separated	yes	200	100	100
Osime	Nigeria	PR	6	1984-1987		no separation		no separation		No	all had 5 days	106	54	51
Oncu	Turkey	RC	6	1988-1990		26.6 (7-64)	22.2 (6-70)	24-16	23-17	Yes	no	80	40	40
Chaudhury	Pakistan	PR	6	1999-2003		unable to separate		45-55	47-53	Yes	NS	677	295	382
Dass	Oman	PR	7	1986-1987	9m	NS	NS	NS	NS	No	yes	130	48	48
Street	USA	RC	6	1981-1986		NS	NS	NS	NS	Mixed groups	yes	886	87	799
Khan	Nepal	PR	7	2001-2007	6m	29.98	30.78	48-22	58-27	No	yes	150	70	80
Minhas	Pakistan	QE	6	2007-2008	20d	25	25	16-14	17-13	Yes	NS	60	30	30
Chalya	Tanzania	PR	6	2009-2010		26.28	24.12	20-23	21-23	Yes	yes	87	44	43
Jamal	Pakistan	RC	6	2006-2007	14d	22.92± 8.57	20.9± 6.23	NS	NS	Yes	yes	80	40	40
												4037	1501	2501

PR Prospective Randomized, R Retrospective, RC Retrospective Case Control, QE Quasi-experimental, NOS Newcastle-Ottawa score, NS Not stated.

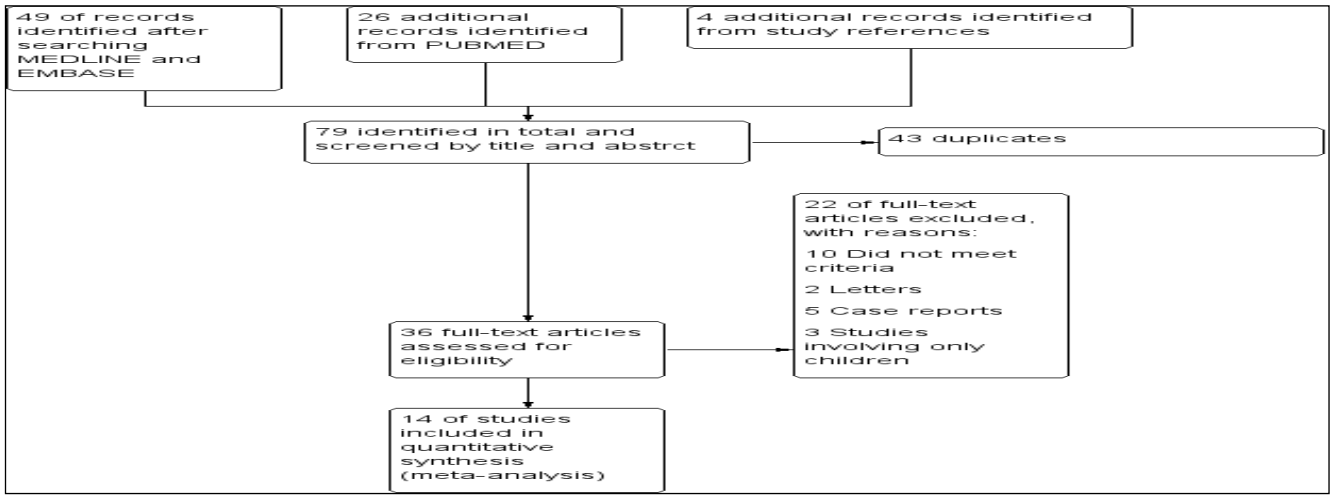

Figure 1: Study design.

Study and patient characteristics

The characteristics of the included 14 studies are summarized in Table 1. There was no overlap of study populations in the included studies. Half the studies comprised retrospective analysis with the rest prospective randomized studies. This encompassed a combined patient population of 4,037, with 1,501 in the stump inversion group and 2,501 in the stump ligation group. Reported post-operative complications consisted of wound infections, total abdominal sepsis, bowel

obstruction, pelvic abscess formation and re-operation. Seven studies excluded perforated appendicitis, whilst two studies separated the groups, with the remainder either failing to report or categories by this operative finding. Use of prophylactic antibiotics was explicitly stated in seven studies.

Outcome measures

Wound infection and total infective complications

Thirteen studies reported data on post-operative wound infection and total infective complications. The incidence of wound infection was 2%-27% in the stump inversion group and 0-30% in the simple ligation group. The analysis of pooled data showed no significant differences in the risk of wound infections and total infective complications between simple ligation and stump inversion; (OR=1.33, CI 0.95-1.85; p=0.09 and OR=1.30, CI 0.93-1.83; p=0.13) respectively (Figure 2 and 3).

After excluding studies without antibiotic prophylaxis there was no difference between inversion or ligation of the appendix stump with respect to either total infective complications (OR=1.03; 95% CI=0.75-1.43, 10 studies) or surgical site infection (OR=1.07; CI=0.78-1.47; 10 studies) (Figure 4 and 5).

Table 2: Results of included studies.

	Outcomes															
	Dichotomous												Continous			
	Wound Sepsis		Pelvic Abscess		Total abdominal septic complications		Adhesive Ileus		Re-operation		Faecal Fistula		Operative time		LOS	
Author	Inverted (n)	Ligated (n)	Inverted (n)	Ligated (n)	Inverted (n)	Ligated (n)	Inverted (n)	Ligated (n)	Inverted (n)	Ligated (n)	Inverted (n)	Ligated (n)	Inverted (n)	Ligated (n)	Inverted (n)	Ligated (n)
Watters	11	8	NS	NS	11	8	0	1	0	1	NS	NS	NS	NS	4	4
Sinha	34	25	2	1	36	27	3	1	NS	NS	NS	NS	NS	NS	8.6	7.1
Engst-rom	21	23	NS	NS	21	23	6	1	NS	NS	NS	NS	45	40	4.9	4.6
Misgar	10	5	3	1	13	6	2	0	NS	NS	1	0	NS	NS	6	4
Lavo-nius	2	2	1	1	3	3	NS	NS	NS	NS	NS	NS	P<0.0004 LONGER		P=0.01 LONGER	
Osime	5	3	0	0	5	3	0	0	0	0	0	0	50	42	7.6	7.2
Oncu	7	6	0	0	7	6	0	0	0	0	0	0			5.62	6.44
Chaudh ury	19	21	0	0	19	21	0	0	NS	NS	NS	NS	NS	NS	NS	NS
Dass	1	0	0	0	1	0	0	0	NS	NS	NS	NS	NS	NS	NS	NS
Street	NS	NS	NS	NS			5	0 / 106	5	0	NS	NS	NS	NS	same/ NS	same/ NS
Khan	19	24	0	0	19	24	0	0	NS	NS	0	0	NS	NS	5.5	5.4
Minhas	4	2	0	0	4	2	0	0	NS	NS	0	0	NS	NS	NS	NS
Chalya	2	1	0	0	2	1	0	0	NS	NS	NS	NS	45.3± 36.1	30.6± 33.4	6.9 ±0.8	6.3± 12.2
Jamal	6	9	0	0	6	9	0	0	NS	NS	NS	NS	NS	NS	NS	NS

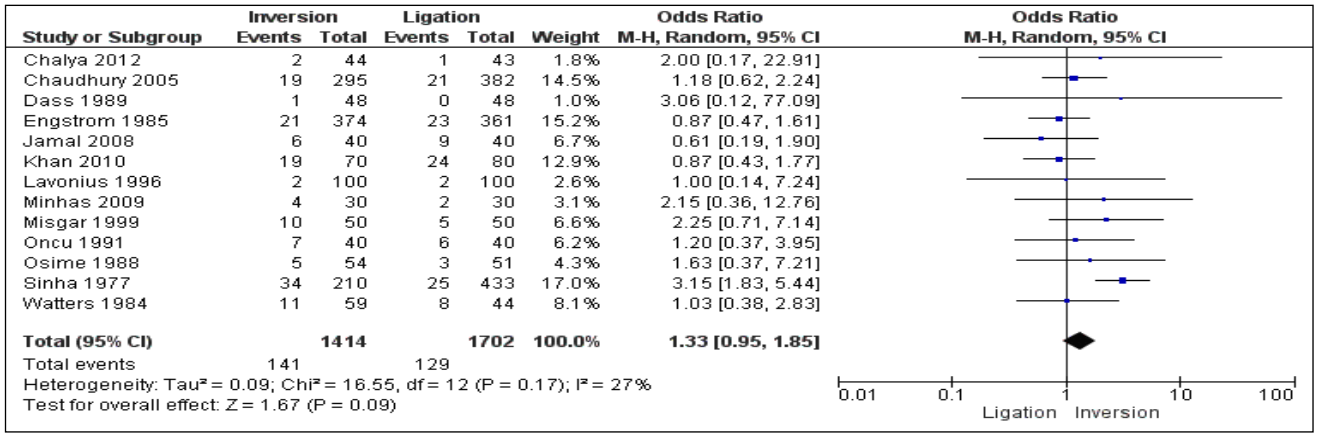

Figure 2: Wound infection.

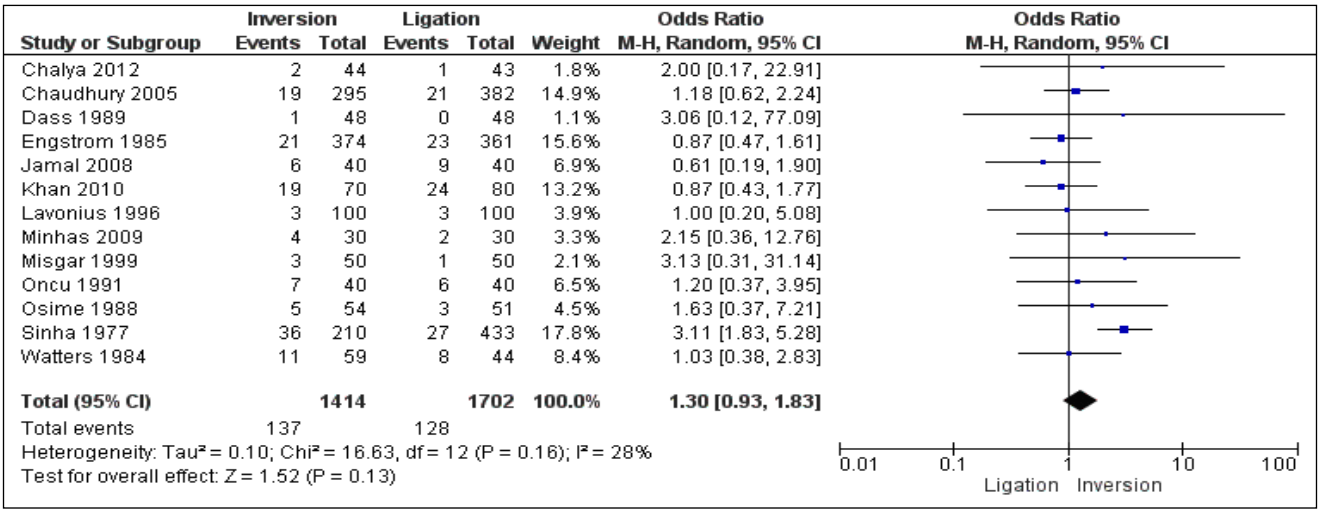

Figure 3: Total infective complications.

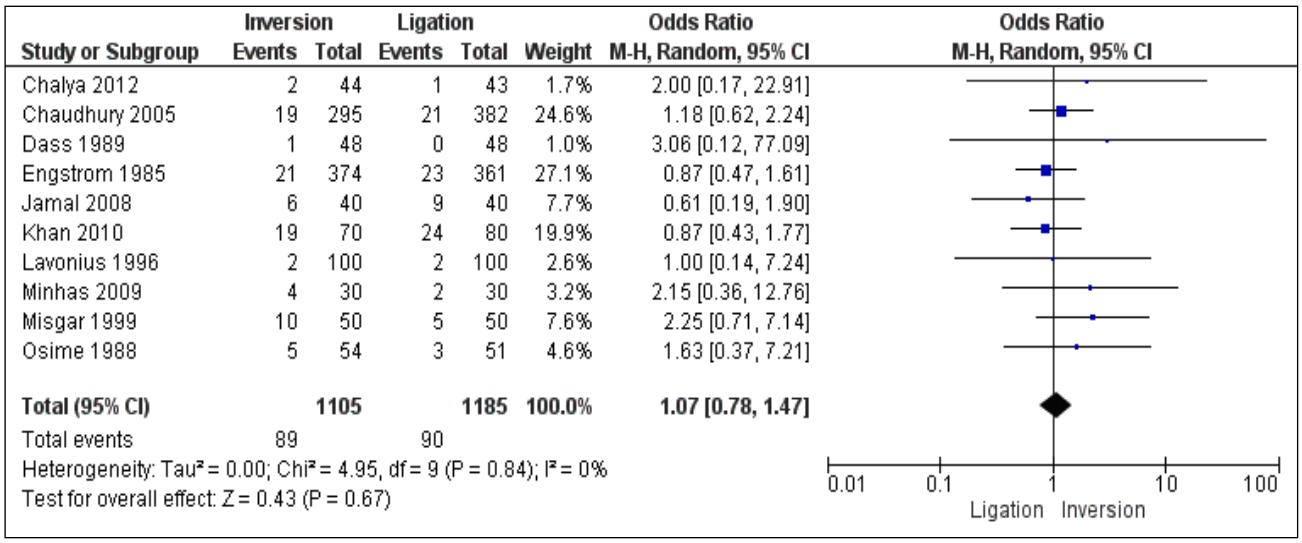

Figure 4: Wound infection excluding studies without antibiotic prophylaxis.

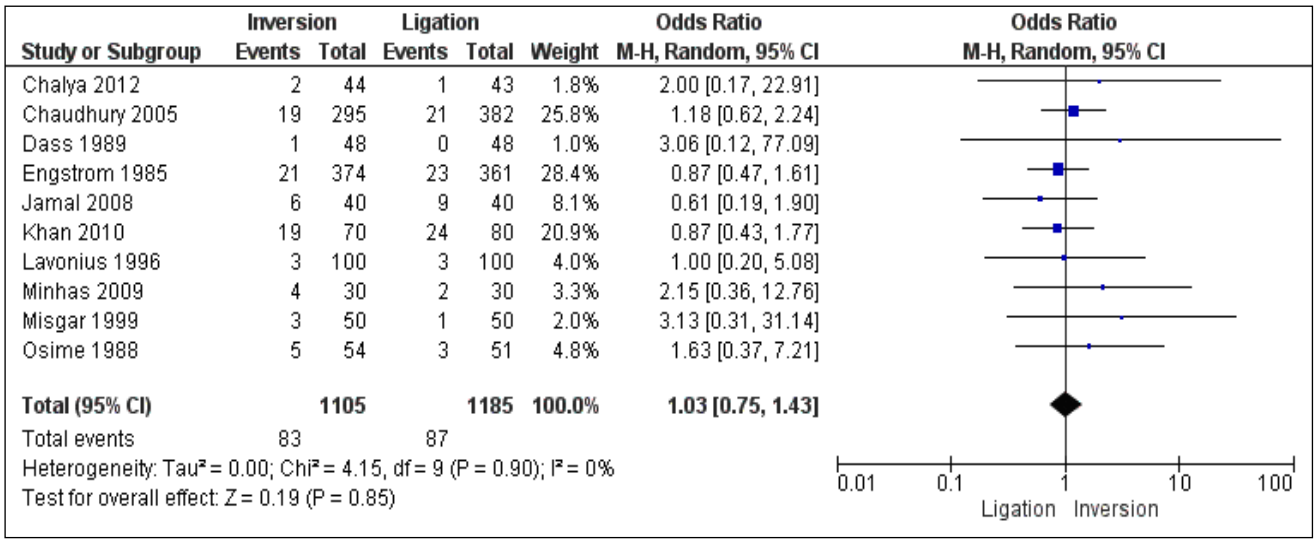

Figure 5: Total infective complications excluding studies without antibiotic prophylaxis.

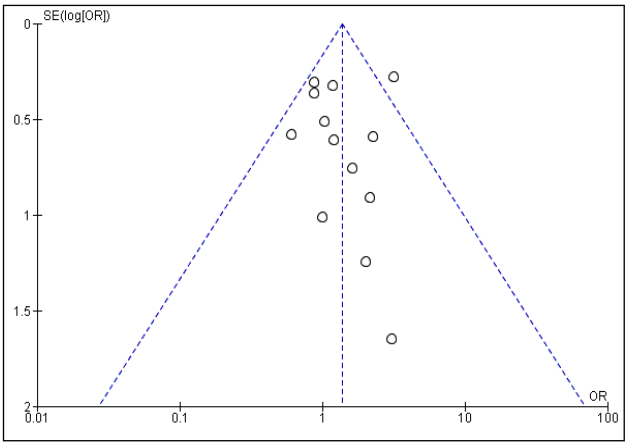

Figure 6: Wound infection funnel plot.

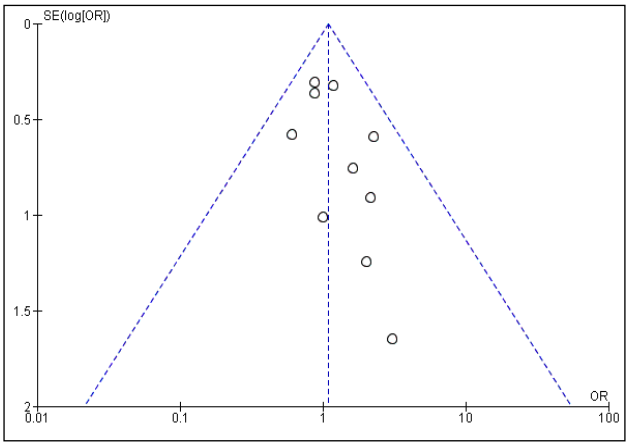

Figure 8: Wound infection excluding studies without antibiotic prophylaxis funnel plot.

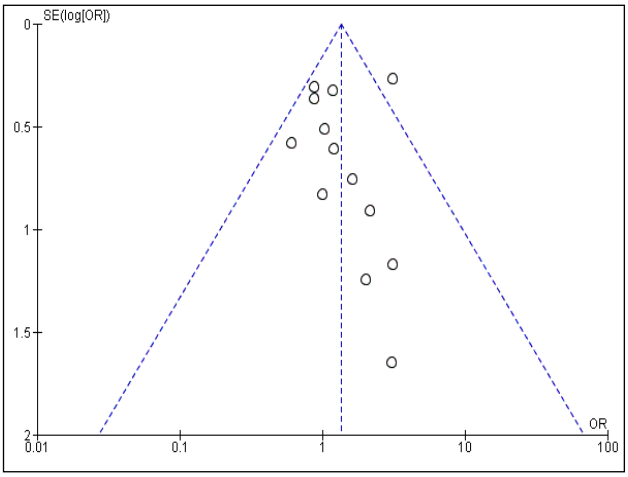

Figure 7: Total infective complications funnel plot.

However, funnel plot revealed an outlier in both the wound infection and total infective complications data (Figure 6 and 7).

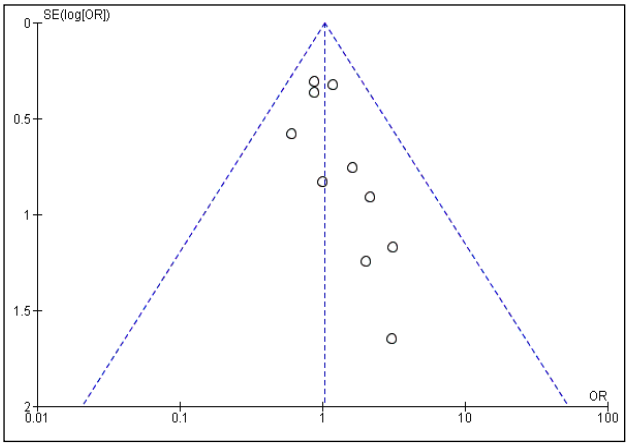

Figure 9: Total infective complications excluding studies without antibiotic prophylaxis funnel plot.

After excluding studies without antibiotic prophylaxis, the results were homogenous for both complications as outlined by the funnel plots (Figure 8 and 9).

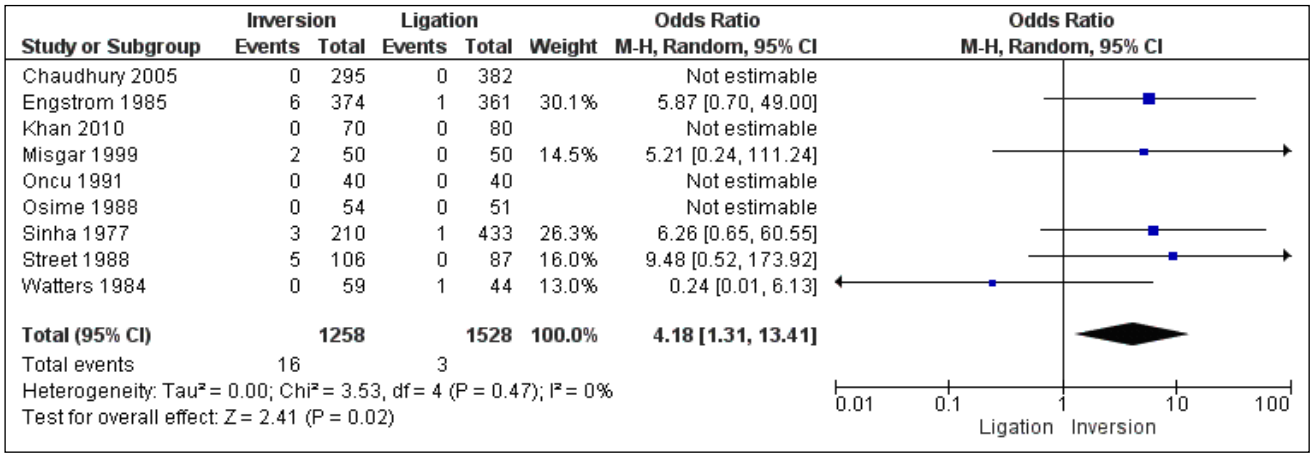

Figure 10: Small bowel obstruction.

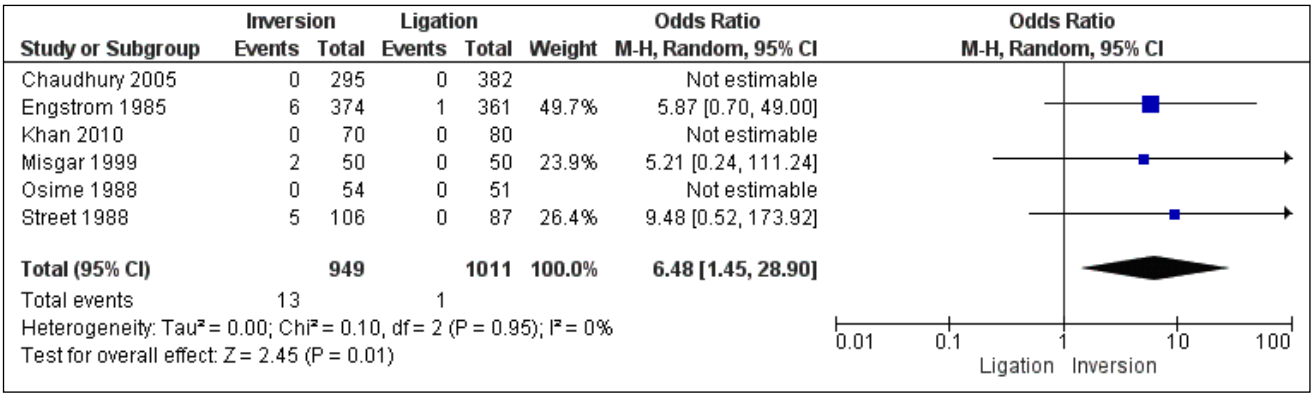

Figure 11: Small bowel obstruction excluding studies without antibiotic prophylaxis.

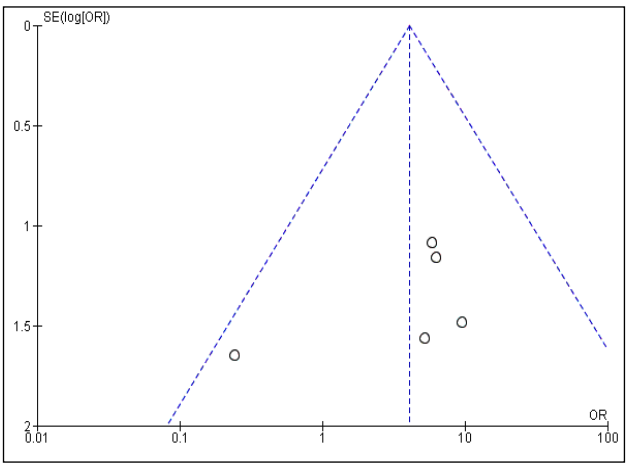

Figure 12: Small obstruction funnel plot.

Small bowel obstruction

The analysis of the pooled data suggests that stump inversion increased the risk of post-operative small bowel obstruction compared to simple ligation of the stump (OR=4.18, CI=1.31-13.41; p=0.02; 9 studies). Excluding studies which failed to report on prophylactic antibiosis increased the significance of this result (OR=6.48, CI=1.45-28.9; p=0.01) (Figure 10 and 11). Funnel plots revealed no outliers in either analysis (Figure 12 and 13) and despite the lower number of studies in this meta-analysis compared to other outcome measures there was low heterogeneity (tau2=0.00; i2=0%) identified, though the extremely low overall event numbers in either group should be noted.

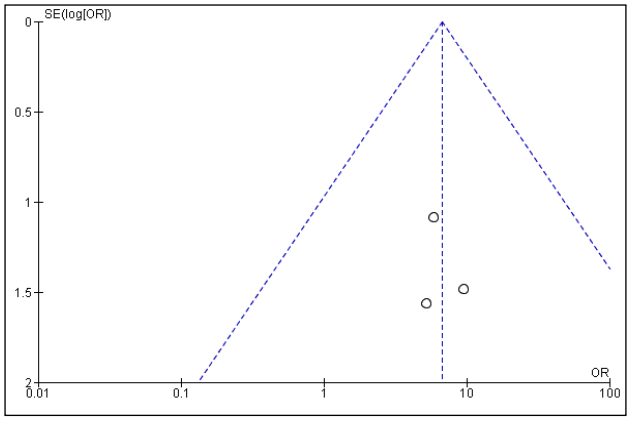

Figure 13: Small bowel obstruction excluding studies without antibiotic prophylaxis funnel plot.

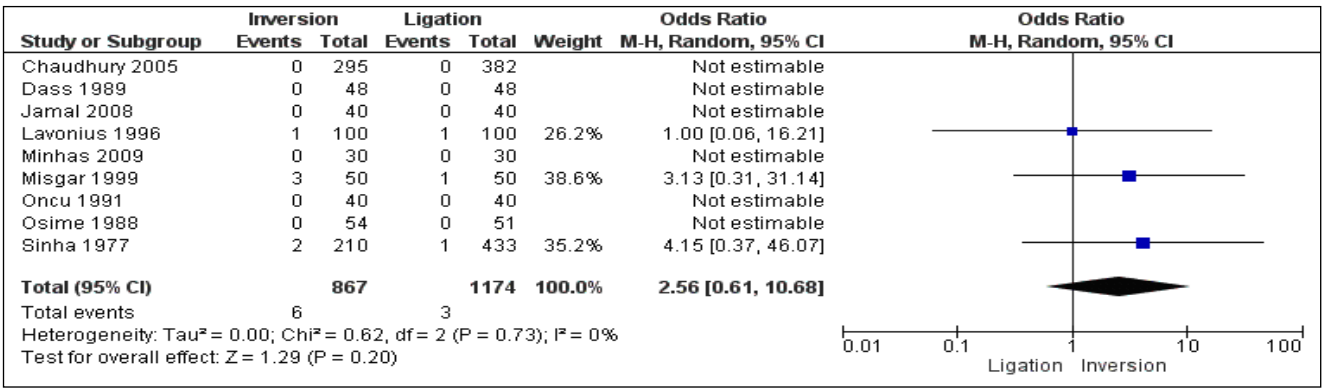

Figure 14: Pelvic abscess formation.

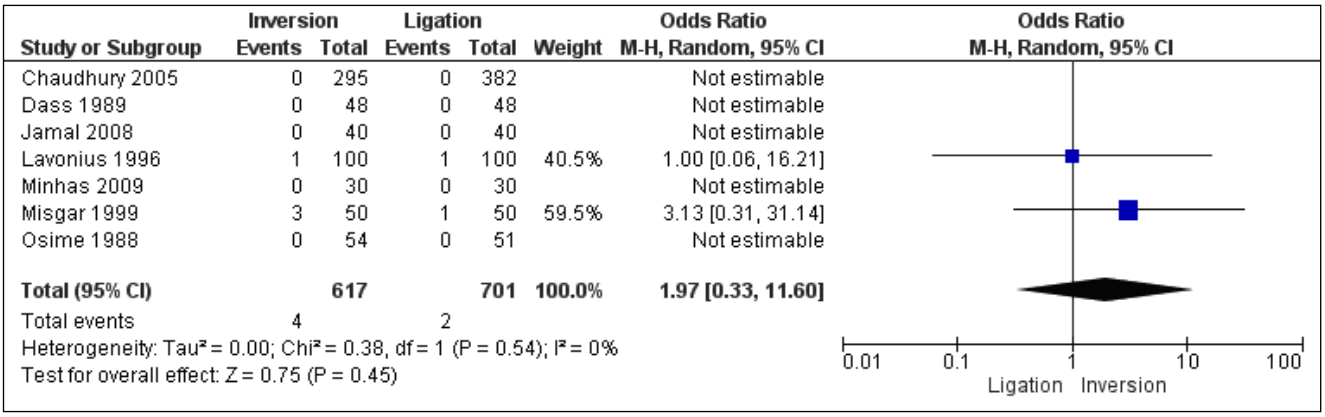

Figure 15: Pelvic abscess formation excluding studies without antibiotic prophylaxis.

Pelvic abscess formation

Nine studies reported data on pelvic abscess formation. Analysis showed no significant difference between the two groups with (OR = 2.56, CI 0.61-10.68, 9 studies) or without antibiotic prophylaxis (OR = 1.97, CI 0.33-11.60, 7 studies) (Figure 14 and 15). Funnel plots revealed no outliers.

DISCUSSION

Open appendicectomy remains a widely performed procedure despite the increasing popularity of laparoscopic surgery in the modern era. This had led to potential differences in surgical management of the appendix stump between open surgery where inversion is commonplace and laparoscopic appendicectomy where routine practice typically involves just simple ligation with an endo-loop or slipknot.

Inversion or invagination of the appendix stump is widely performed during open appendicectomy. This common operative step pre-dates the antibiotic era. Initial aims of invagination were to control haemorrhage, reduce adhesion formation and prevent peritoneal contamination and subsequent sepsis.[7] In this meta-analysis there were a total of 14 studies with a combined patient population of 4,037 patients included. Our analysis examined the outcome measures of interest to the operating surgeon, including: wound infection, pelvic abscess, total abdominal sepsis and post-operative small bowel obstruction. Neither stump inversion or simple ligation conferred any advantage towards avoiding infective complications with wound infection, pelvic abscess and total abdominal sepsis being equivalent in both groups.

An early report from the pre-antibiotic era of surgery reports intramural caecal abscess following invagination of the appendix stump.[10] A later retrospective study by Sinha indicated a higher rate of wound infection, intramural abscess and adhesions following inversion of the appendix stump.[6] More recently there have been five prospective trials comparing invagination of the appendix stump with ligation or transfixion. Of these, three found no difference in complication rates with either technique.[11-13] The largest study by Oncu reported a higher rate of adhesions requiring re-operation when the stump is invaginated, and a significantly shorter operating time when the appendix base is simply ligated.[14] Jacobs in 1991 reported an elevated wound infection rate following stump invagination in contrast with ligation only.[15] The literature suggests that invagination is at best equivalent to simple ligation and may both prolong the operation and be associated with increased risk of developing post-operative complications.

Worth noting that our meta-analysis differentiated between studies that administered and did not administer antibiotic prophylaxis. With regards to infective complications we found no statistical significance in either group. Early studies where antibiotic use was not prevalent may have identified differences that are of no further clinical relevance. Additionally, not all the studies excluded perforated appendicitis which would adversely affect the outcomes for each group. This reflects an early literature paucity of modern RCT studies.

The most significant finding of this meta-analysis is the identification of stump inversion as a possible risk factor for the development of post-operative small bowel obstruction. The significance of this increased after exclusion of studies not administering prophylactic antibiotics and has not been reported before. Kohler et al suggested there is actually an increased incidence of adhesions with stump inversion; Engstrom and Fenyo also found that adhesional obstruction was more common.[7,8] A further hypothesis for this finding could be that stump invagination can lead to intussusception which can lead to bowel obstruction. Cleland (1953) reported 6 cases of intussusception following open appendicectomy in the literature.[16] Cleland and Mayo (1934) stated that this was why they did not practice invagination of the stump.[16,17] Thus, it can be proposed that simple ligation

as performed in laparoscopic appendicectomy may be the preferred approach for open appendicectomy.

The remnant inverted appendix stump may also deform the caecal wall, creating an intra-luminal indentation which, as in our case, can mimic true pathology such as a caecal polyp or cancer. Multiple cases have been reported with colonoscopy and CT virtual colonograph.[18-20] At colonoscopy, an inverted stump may have the appearance of a smooth sessile polyp with an absent appendix orifice.[21] Pathological findings in the caecum need colonoscopy and biopsy to obtain a definitive diagnosis. This may lead to unnecessary endoscopy with its associated risk of bleeding and perforation. The main limitation of this meta-analysis is the quality of the comparative analysis possible in view of the scarcity of the studies available that documented on them and the low incidence in which they occur (for example, re-operation rates or faecal fistulae). Larger studies would be valuable to draw any definitive conclusions on the effects of stump ligation or stump inversion. Furthermore, the quality of the studies was not optimal for accurate analysis. We were unable to reliably determine which methods of randomisation were used in the original studies and there was lack of double blinding of participants. We attempted as best we could to dutifully select studies that allowed for the most homogenous and comparable group of patients. We included 7 prospective RCTs vs 7 case control series or retrospective analysis. We also included older studies from low impact factor journals due to limited number of modern high quality RCTs.

Additionally, follow up data was not optimal, only 4 studies included this information and the maximum follow up was 9 months, this is less than optimal to fully assess the sequelae of the two techniques. Lastly, attrition rate was seldom stated, this is a weakness as attrition is a ubiquitous problem in RCTs and other studies that can cause biased estimates of the treatment effect, reduce statistical power, and restrict the generalizability of results.

There are 2 previously published meta-analyses looking at similar data. However, they were only able to look at two outcome measures and included less studies.

Meta-analysis by Gravante et al involved 7 studies and only 1,468 patients, Qian et al included 11 studies and 2,634 patients, compared to our 14 studies and 4,037 patients. Gravante concluded that compared to the simple ligation the invagination of the stump increased the risks of postoperative ileus and does not decrease the wound infection rate.[22] The clinical results of Qian revealed that simple ligation was significantly superior to stump inversion with a decreased risk of postoperative ileus.[23]

Additionally, there was no mention of prophylactic antibiotic use. Antibiotic prophylaxis plays an essential role in the prevention of wound infections. Burke established the basis for the use of antibiotics peri-operatively and the efficacy of antibiotic prophylaxis has been previously shown to be significant.[24] The hypothesis has been reconfirmed by clinical studies performed by Polk and Stone.[25,26] Open appendicectomy for non-perforated appendicitis is largely classified as a clean-contaminated procedure and it is widely accepted that antibiotic prophylaxis is warranted in these cases.

CONCLUSION

To conclude, this meta-analysis is the first to examine the full spectrum of complications and specific outcomes following appendicectomy taking into account the use of antibiotics. Our study has not identified any benefit to the continued practice of inverting the appendix stump during open appendicectomy. Furthermore, our analysis suggests that there may be an association between post-operative small bowel obstruction and inversion of the appendix stump. Our opinion would be that given a lack of benefit, a longer operating time and risk of misdiagnosis of caecal pathology in later life, that inversion should be avoided as surgical step where possible. This will also unify practice during appendicectomy between open and laparoscopic approaches in an evidence based manner.

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Ethical approval: Not required

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