



The use of polymeric clips in securing the appendiceal stump during laparoscopic appendicectomy: a systematic review

Stephen Robert Knight¹ · Abdulla Ibrahim² · Nav Makaram² · Pradeep Patil² · Michael Samuel James Wilson² 

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Abstract

Purpose A key step during laparoscopic appendicectomy is securing the appendiceal stump. This has traditionally been achieved using vicryl endoloops, but increasing evidence suggests that the use of polymeric clips (Hem-o-lok) may be a safe and viable method. Current evidence for its clinical use in laparoscopic appendicectomy is unknown. We performed a systematic review of the literature examining the clinical outcomes of laparoscopic appendicectomy using polymeric clips compared to other methods of stump closure.

Methods A systematic literature review based on PRISMA guidelines was performed using MEDLINE, PubMed, EMBASE and Cochrane library databases between 2000 and 2017. All studies analysing appendiceal stump closure during laparoscopic appendicectomy using polymeric clips compared to other methods of stump closure were included. The methodological quality of the included studies was assessed using the Cochrane Handbook for Systematic Reviews. The review was registered with the PROSPERO register of systematic reviews.

Results Ten studies were included, involving 702 patients, 7 of which were prospective studies and 1 a randomised control trial. Polymeric clips were found to be the cheapest method (€20.47 average per patient) and also had the lowest rate of complications (2.7%) compared to other commonly used closure methods. Meanwhile, operative time and duration of in-patient stay were similar between groups.

Conclusions Current evidence suggests that polymeric clips are an effective and cost-efficient method for stump closure in laparoscopic appendicectomy for acute appendicitis. Further high-quality evidence is required before polymeric clips can be recommended as the gold standard for appendiceal stump closure.

Keywords Appendicectomy · Stump closure · Polymeric clips

Introduction

Acute appendicitis is the most common indication for emergency abdominal surgery with a lifetime incidence between 8 and 16% [1, 2]. Laparoscopic appendicectomy (LA) was first reported in 1983 [3] and is now accepted as the primary method of choice for the surgical management of acute appendicitis [4].

A key step during LA is closure of the appendiceal stump. The most commonly employed methods include use of endoscopic ligatures (EL) [5] or a gastrointestinal laparoscopic stapler [6]. Others include use of a harmonic scalpel, bipolar coagulation or metal clips [7].

More recently, an alternative method has been reported and involves the use of a nonabsorbable polymer locking ligation system (e.g., Hem-o-lok[®] Teleflex, North Carolina, USA) to secure the appendiceal stump [8, 9]. The advantage

✉ Michael Samuel James Wilson
michaelwilson3@nhs.net

Stephen Robert Knight
stephenknight1@nhs.net

Abdulla Ibrahim
abdulla.ibrahim@nhs.net

Nav Makaram
n.makaram@nhs.net

Pradeep Patil
pradeepatil@nhs.net

¹ Monklands Hospital, Airdrie ML6 0JS, UK

² Ninewells Hospital and Medical School, Dundee DD1 9SY, UK

of this method is the ease of application, low cost and potentially reduced operative time [9]. However, to our knowledge, no systematic review has been performed formally examining the use of polymeric clips (PC) in appendiceal stump closure compared to other, more commonly employed methods.

In this study, we aim to systematically review the existing literature examining the evidence base for PC compared to other methods of stump closure in LA. Outcomes to assess will include operative time, length of stay and post-operative complications. A cost analysis will also be performed.

Materials and methods

A systematic literature review was conducted using the Standard Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [10]. The review was registered with the PROSPERO register of systematic reviews. A literature search was undertaken using MEDLINE, PubMed, EMBASE and Cochrane library databases between 1st January 2000 and 31st December 2017 with the medical subject heading (MeSH) search terms ‘polymeric clip’ OR ‘Hem-o-lok’ AND ‘appendicitis’ OR

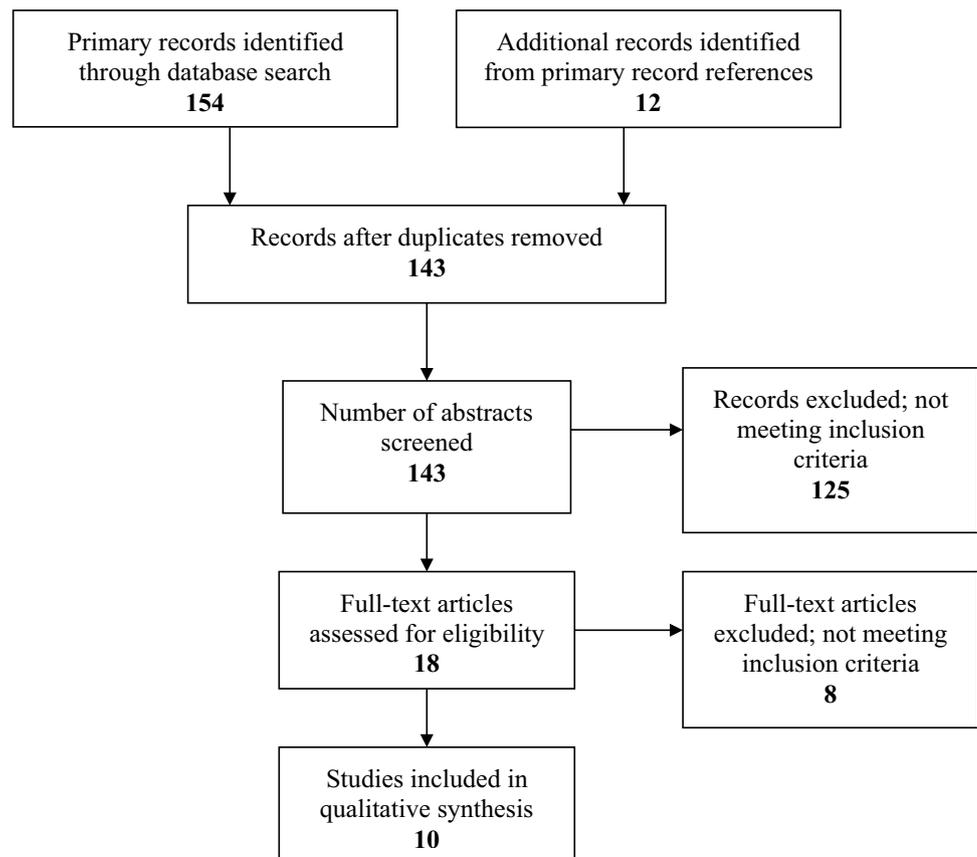
‘appendectomy’ O R ‘appendicectomy’ (Fig. 1). No protocol has previously been published in relation to this study.

Limits selected were publication type ‘articles’, studies in the English language and human subjects. Inclusion criteria were studies that assessed appendiceal stump closure during LA using PC compared to another method of stump closure. Articles examining the use of PC only, together with conference abstracts, letters, editorials and case reports were excluded.

Following the initial literature search, abstracts were screened independently by two authors (SK and MW), with any differences resolved by consensus between authors. Additional studies, not included in the initial literature search, were identified by manual screening of included article reference lists (Fig. 1).

The following variables were recorded from each article: study design, patient numbers and methods of appendiceal stump closure. For each method used within the study, the following were collected, if available: operative time, length of hospital stay, complications (intra- and post-operative) and cost. To enable comparison of costs between studies, quoted costs were converted into the equivalent value in Euros using the average conversion rate for the year of publication [11]. The methodological quality of the included

Fig. 1 PRISMA flowchart of literature search



studies was assessed using the Cochrane Handbook for Systematic Reviews [12].

Outcomes were converted to means according to Hozo et al. [13] and weighted means were calculated to enable comparison between groups. When performing statistical analyses, differences between methods of stump closure were analysed using ANOVA with use of post hoc Tukey analysis. Percentages between groups were compared using Chi squared test. Data were analysed using statistical package R v3.3.1 (Vienna, Austria) [14], with *P* value < 0.05 considered statistically significant.

Results

Overview

The literature search results are summarised in Fig. 1. 154 studies were initially identified using the search terms with an additional 12 references. After screening, 23 studies were excluded due to duplication, whilst a further 133 studies were excluded either due to irrelevance or failing to meet inclusion criteria. Ten full-text studies [8, 9, 15–22]

compared the use of PC clips for stump closure versus at least one other method (Table 1).

Within these studies, PCs were compared to several other methods of stump closure; six studies compared the use of PC to EL, two to endostaplers and one study to intra-corporal knots, while one study investigated the use of both EL and endostaplers compared to polymeric clips. Six studies were prospective, three retrospective and one randomised controlled trial (RCT).

The majority used adult subjects. One study analysed the use of PC in children [18]. On average, 33 patients were used for each treatment group (range 14–68). Table 2 demonstrating the cohort sizes across all studies. A formal meta-analysis was not performed because of obvious clinical heterogeneity between studies and the lack of comparative analyses.

Critical appraisal

The only RCT, by Colak et al. [17], was at high risk of bias due to the absence of blinding and an adequate power calculation. This study was given an evidence level of 2b (Table 1). This was the highest level of evidence within the included studies, with the remaining studies graded as level

Table 1 Studies comparing the use of polymeric clips to at least one other method of stump closure in laparoscopic appendicectomy

(a) Study	Type of study	Level of evidence	Risk of bias	Comparison	Subjects							
					PC	EL	ES	ICK				
Delibegovic et al. [7]	Prospective	Level 4	High	EL	28	24	–	–				
Partecke et al. [14]	Prospective	Level 4	High	ES	26	–	56	–				
Hue et al. [15]	Prospective	Level 4	High	EL	39	66	–	–				
Colak et al. [16]	RCT	Level 2b	High	EL	26	27	–	–				
Akbiyik et al. [17]	Prospective	Level 4	High	EL	28	21	–	–				
Simsek et al. [18]	Prospective	Level 4	Moderate	EL	30	30	–	–				
Polat et al. [19]	Retrospective	Level 4	High	ICK	48	–	–	44				
Jenwitheesuk et al. [20]	Retrospective	Level 4	Moderate	EL	68	23	–	–				
Hanssen et al. [8]	Retrospective	Level 4	High	ES	14	–	14	–				
Delibegovic [21]	Prospective	Level 4	High	EL&ES	30	30	30	–				
(b) Study	Operative time (min)				Length of stay (days)				Cost			
	PC	EL	ES	ICK	PC	EL	ES	ICK	PC	EL	ES	ICK
Delibegovic et al. [7]	39	48	–	–	2.2	2.2	–	–	€76.90	€88.50	–	–
Partecke et al. [14]	65	–	54	–	3.8	–	3.1	–	€19.94	–	€356.43	–
Hue et al. [15]	NA	NA	–	–	5.3	5.2	–	–	€21.98 ^a	€51.35 ^a	–	–
Colak et al. [16]	65	76	–	–	2.1	2.5	–	–	€22.59 ^a	€90.37 ^a	–	–
Akbiyik et al. [17]	38	44	–	–	3.2	3.4	–	–	€28.75 ^a	€87.34 ^a	–	–
Simsek et al. [18]	40	50	–	–	1.9	2.1	–	–	NA	NA	–	–
Polat et al. [19]	26	–	–	33	1.1	–	–	1.4	NA	–	–	NA
Jenwitheesuk et al. [20]	38	66	–	–	2.5	3.2	–	–	NA	NA	–	–
Hanssen et al. [8]	54	–	63	–	2.0	–	2.8	–	NA	–	NA	–
Delibegovic [21]	43	46	40	–	2.1	2.1	2.0	–	€4.75	€57.70	€230.77	–

Table 2 Combined study analysis comparing outcomes in appendiceal stump closure using various methods

Device	Subjects (<i>n</i>)	Average operative time (minutes)	Complication rate (%)	Average length of stay (days)	Average cost
Polymeric clips	337	37	2.7	2.4	€20.47
Endoloop	221	39	5.0	2.6	€69.96
Intra-corporeal knot	44	33	13.6*	1.4	–
Endostapler	100	51	5.0	2.7	€153.26 ^{†,‡}

Weighted means calculated with statistical analysis performed using ANOVA with post hoc Tukey's test
 * $P < 0.05$ vs. polymeric clip group, [†] $P < 0.01$ vs. polymeric clip group, [‡] $P < 0.01$ vs. endoloop group

4 due to their case series nature or absence of an appropriately matched control group.

Operative time and length of stay

Mean operative times were similar across PC (37 min; range 26–65), EL (39 min; 44–76), endostapler (51 min; 40–63) and intra-corporeal knot (33 min, no range) groups [$F(2.17) = 1.078$, $P = 0.365$]. One study failed to report operative time. Marked variation existed across studies for in-patient stay, ranging from 1.1 to 5.3 days. For the PC group, mean length of stay was 2.4 days (range 1.1–5.3) compared to 2.6 days (2.1–5.2) for EL and 2.7 days (2.0–3.1) when using endostaplers. In the one study exploring intra-corporeal knots, the average length of stay was 1.4 days. In-patient stay was similar across all groups [$F(2.19) = 0.205$, $P = 0.816$].

Complications

The average complication rate was 4.4% (Table 2), however varied depending upon the method of stump closure [$\chi^2(3) = 11.54$, $P = 0.009$]. PC demonstrated the lowest rate of complications (2.7%), whilst the single study involving intra-corporeal knots had the highest rate (13.6%). EL and endostaplers had a similar complication rate to PC. Table 3 summarises the complications across all studies.

Operative cost

Cost varied greatly between studies and the method of stump closure, ranging from €4.75 to €356.43 (Table 1). Four studies did not report operative cost. PC had the lowest reported cost of €20.47 per patient (range €4.75–€28.75). EL cost €69.96 per patient (€51.35–€90.37), followed by the endostapler method €153.26 per patient; €230.77–€356.43; $P < 0.001$ compared to PC and EL groups; [$F(2.12) = 42.87$, $P < 0.001$]. The cost difference between PC and EL groups was similar [$F(2.12) = 42.87$, $P = 0.128$].

Table 3 Complications occurring following laparoscopic appendectomy according to stump closure method

Complication	PC	EL	ES	ICK
Intra-operative bleeding from mesoappendix	3	0	1	0
Intra-abdominal collection	1	1	1	0
Intra-operative bleeding from staple line	0	0	1	0
Bleeding from port site	1	0	0	0
Intra-abdominal haematoma	0	0	1	0
Intra-abdominal peritonitis	0	0	1	0
Wound infection	5	2	2	4
Nonsurgical complication	1	1	0	0
Post-operative ileus	0	0	0	2

PC polymeric clip, EL endoloop, ES endostapler, ICK intra-corporeal knot

Discussion

A number of methods have been described for closure of the appendiceal stump during LA, with the most commonly employed methods currently being EL or use of a stapling device [7]. PCS are easily applied and do not require a steep learning curve. They are widely used in a variety of surgical procedures primarily for vessel and tissue ligation such as cholecystectomy, nephrectomy and colonic resection [23, 24]. Results in animal studies have concluded that stapling devices and PC, when applied to the appendiceal stump produce a milder post-operative inflammatory change when compared to EL [25].

Our review has identified PC as an equivalent and safe method in securing the appendiceal stump during LA. We have not identified a difference in operative time, complication rate or in-patient stay. It also has potential as a more cost-effective approach.

Operative time was similar between all groups; however, the endostapler group had a longer mean operative time of 52 min. Of the three studies involving endostaplers, the retrospective study had the longest operative time at 63 min compared to 40 and 54 in the prospective studies. The retrospective nature raises the possibility

of selection bias, with difficult appendicectomies (e.g., necrotic appendix base or caecal perforation) requiring the use of the endostapler to secure the caecal pole [6]. Cost may be the limiting factor that prevents routine use of endostaplers and in many centres, such as our own, an endostapler is only utilised in the most severe cases of appendicitis. More recent studies have concluded that the use of mechanical devices (staplers or PC) during LA saves 9 min of operating time when compared to EL [26, 27].

The single paediatric study reported the length of PC application took 1 min versus the 5 min of using EL [18] and it is well described that EL take longer to deploy [8]. However, this increase in operative time was not demonstrated with pooled data.

Post-operative complication rates were similar across all stump closure methods except for the intra-corporeal knot group. This study had a complication rate of (13.6%) primarily due to wound infections. PC had the lowest complication rate at 2.7%, however, a small but non-significant increase in intra-operative bleeding from the mesoappendix and wound infection was seen with this method.

The incidence of post-operative peritonitis and intra-abdominal collection was low, with only 4 cases identified across 702 patients. It is likely that inadequate stump closure would manifest as either of these two complications [6]. Furthermore, the degree of appendix inflammation and adequacy of laparoscopic washout, which would influence such rates, was not adequately controlled for in the majority of included studies.

Our analysis demonstrated the use of PC as the cheapest method of stump closure, with an average saving of €49.50 compared to EL. Although their values remained statistically similar, a significant saving may still be achieved if PCs were used more frequently in clinical practice.

Operative technique when applying PC varied within studies, with three using only one proximal PC to secure the appendiceal stump [15]. Partecke et al. argue that the length of stump after the first clip is longer when applying two clips, thus increasing the risk of stump necrosis and local abscess formation [15]. However, we did not identify a significant difference in post-operative complications between these two techniques.

The diameter of the appendix base has been identified as a possible limitation of the polymeric clip method, as it is only able to ligate up to 10 mm of tissue [17]. Hue et al. demonstrated polymeric clips ligated an average appendix base length of 9.9 mm, compared to 9.7 mm with EL [16]. However, the maximum length ligated successfully using PC was 11 mm, while EL reached up to 15 mm. Partecke et al. found in individual cases the application of polymeric clips failed, however, the cause for this failure was not identified. No other studies specified the failure rate for PC.

Conclusions regarding the choice of stump closure method in the presence of severe appendicitis are hard to draw due to some studies failing to account for the severity of appendicitis in their methods [8, 16, 18]. PCs were shown to be effective even in the presence of inflamed appendiceal bases [15].

The studies contained within this review were underpowered, with an average of 33 patients per group within each study. A power calculation indicates at least 126 patients are required to determine a significant difference in operating time with appropriate precision ($\alpha=0.05$, $\beta=0.80$). The only RCT identified contained less than 30 patients per treatment arm, whilst the largest group contained 68 patients.

In addition, significant bias may exist. The lack of randomisation may introduce selection bias, such as surgeon preference or the selection of a particular stump closure method dependent on intra-operative findings. For example, in cases of severe appendicitis, surgeon preference may be to select the endostapling method.

In the future, a suitably powered RCT comparing PC to EL and/or laparoscopic stapling devices is required. Insufficient evidence exists to conclude whether PCs are currently the appendiceal stump closure method of choice. The heterogeneity of included studies and level of evidence precluded the performance of a meta-analysis. However, the literature has identified the potential of PC and high-level evidence is now required to confirm our findings.

Conclusion

Our review suggests that PCs are a safe and cost-effective method of stump closure during LA. However, further adequately powered studies including RCTs are required before firm conclusions can be drawn.

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Compliance with ethical standards

Conflict of interest Stephen Robert Knight declares that he has no conflict of interest. Abdulla Ibrahim declares that he has no conflict of interest. Navnit Makaram declares that he has no conflict of interest. Pradeep Patil declares that he has no conflict of interest. Michael Samuel James Wilson declares that he has no conflict of interest.

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