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Prophylactic hemoclips in prevention of delayed post-polypectomy bleeding for ≥ 1 cm colorectal polyps: meta-analysis of randomized controlled trials

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ABSTRACT

Background and aim Studies evaluating the role of prophylactic hemoclips (HC) in prevention of delayed post-polypectomy bleeding (DPPB) have reported conflicting results. We conducted a meta-analysis of randomized controlled trials (RCTs) to evaluate the role of prophylactic HC placement in prevention of DPPB for polyps ≥ 1 cm in size.

Methods We reviewed several databases to identify RCTs evaluating the role of HC in prevention of DPPB. The outcomes assessed included prevention of DPPB with polyps 1 to 1.9 cm, ≥ 2 cm, any polyp ≥ 1 cm, proximal colon polyps, distal colon polyps, and perforation. We analyzed data using a fixed effect model and reported summary pooled risk ratios (RR) with 95% confidence intervals (CI). We assessed heterogeneity with the I^2 statistic.

Results We included nine RCTs with 4550 patients. For polyps ≥ 2 cm, there was a statistically significantly lower risk of DPPB with use of HC; RR 0.55, 95% CI 0.36, 0.86. There was also a statistically significantly lower risk for proximal colon polyps ≥ 2 cm; RR 0.41 (0.24, 0.70) but no significant difference for distal polyps; RR 1.23 (0.45, 3.32). There was also no significant difference in risk for polyps 1 to 1.9 cm; RR 1.07 (0.59, 1.97). There was no significant reduction in risk of perforation with HC use for any polyp size.

Conclusions Prophylactic HC placement is effective in prevention of DPPB from proximal colon polyps ≥ 2 cm, but of no significant benefit for polyps 1 to 1.9 cm in size or for distal colon polyps ≥ 2 cm.

Introduction

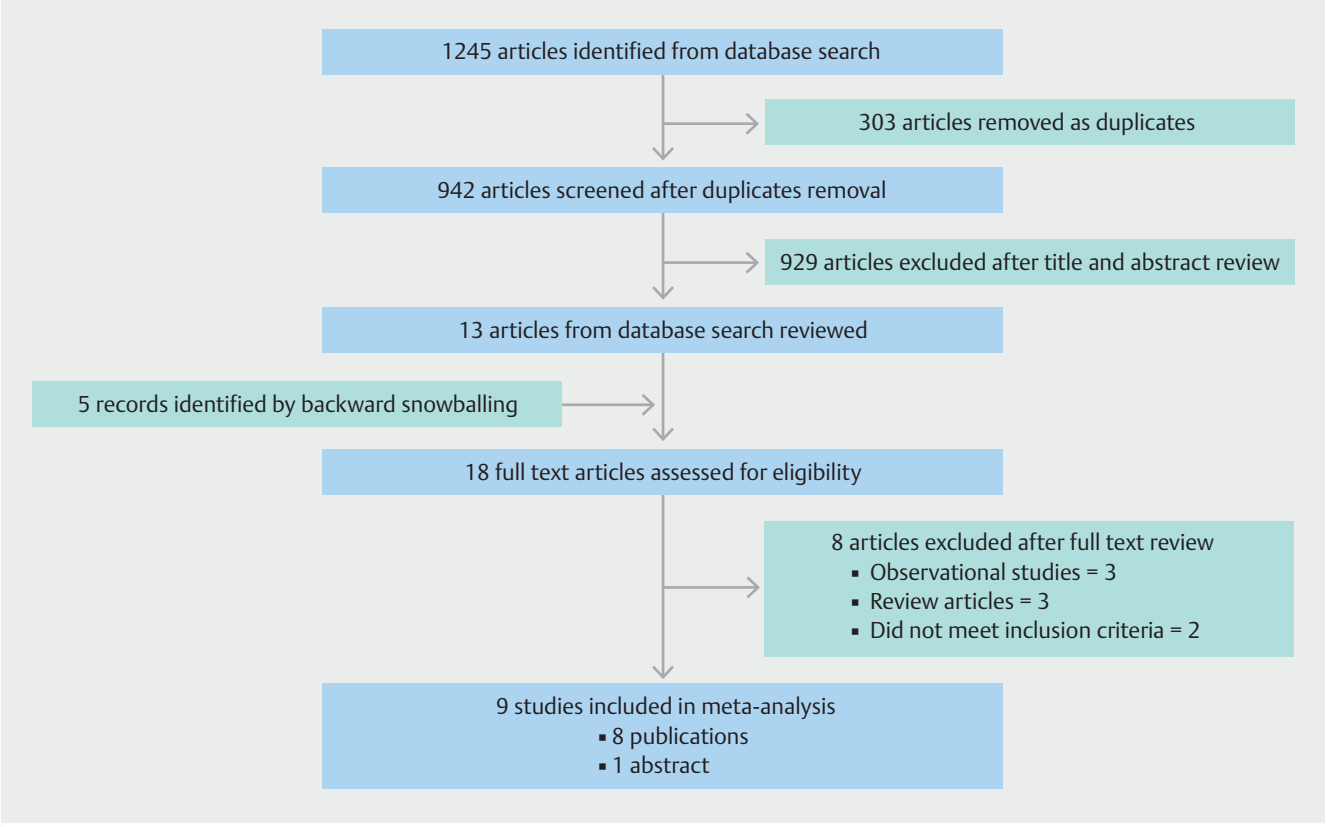
Colonoscopic resection of polyps decreases risk of development of colorectal cancer [1]. Resection of polyps ≥ 1 cm in size is performed by either a conventional snare polypectomy or endoscopic mucosal resection (EMR). Complications of polypectomy include bleeding (2.6/1000), perforation (0.5/1000) and post-polypectomy syndrome (1%) [2–4]. Post-polypectomy bleeding can be immediate (i. e. occurring at time of polypectomy) or delayed, which is typically seen within 14 days of colonosco-

py [5]. Delayed post-polypectomy bleeding (DPPB) is a rare but serious complication that may require hospitalization, blood transfusion, repeat colonoscopy and, rarely, angiographic embolization or surgery [5–7]. Risk factors for DPPB include polyp size > 1 cm, location in the right side of the colon, immediate post-polypectomy bleeding, and use of anticoagulation [8–10]. Prophylactic hemoclip placement after polyp resection has become a common practice for prevention of DPPB but increases total costs. Furthermore, there are only limited data to support their routine use in this setting. Studies evaluating their role in prevention of DPPB have shown conflicting results [11, 12]. There are no guidelines regarding their prophylactic use in the prevention of DPPB, which makes it difficult to identify patients who would be most likely to benefit from their placement. When and how to place hemoclips is decided by individual endoscopists, whose practices may vary widely. Since some studies have shown no benefit of hemoclips in prevention of DPPB [11, 13] and increased costs, their routine use may not be justified. Randomized controlled trials (RCTs) have evaluated the role of hemoclips in prevention of DPPB for colorectal polyps 1 to 2 cm and ≥ 2 cm in size [13–15]. We conducted a meta-analysis of RCTs to evaluate the role of hemoclips in the prevention of DPPB for polyps ≥ 1 cm.

Methods

Data sources and search strategy

We followed the guidelines of Preferred Reporting items for Systematic Review and Meta-Analysis (PRISMA) [16] (**Supplementary Fig. 1**). We performed a comprehensive search of Pubmed, Web of Science, Scopus and Cochrane Database of Systematic Reviews from inception to 10/3/2019. The search was conducted by an experienced medical librarian (T.N.). There was no limitation of language in conducting the search. We used the following key words in conducting the search: "post-polypectomy bleed" OR "delayed post-polypectomy bleed" OR "hemorrhage" OR "bleeding" AND "hemoclips" OR "endoscopic clips" OR "prophylactic clip" OR "endoscopic closure" OR "clips" AND "polypectomy" OR "endoscopic mucosal resection" OR "colonic polyps" OR "polyp removal" OR "polyp resection." Two authors (F.K. and M.A.K.) independently reviewed titles and abstracts of identified studies and excluded those that did not report the effect of hemoclips (HC) in prevention of DPPB for polyps ≥ 1 cm in size. We reviewed the full texts of remaining articles to determine that they meet inclusion criteria and reviewed the references in these articles to identify any additional relevant studies. The search strategy is illustrated in ▶ **Fig. 1**.



▶ **Fig. 1** PRISMA flowchart. From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Inclusion and exclusion criteria

Two authors (F.K. and M.A.K.) independently searched for original studies based on pre-determined inclusion criteria. We included only RCTs that compared prophylactic HC placement with no HC in the prevention of DPPB for polyps ≥ 1 cm in size. Studies included patients older than age 18 years who had at least one polyp ≥ 1 cm in size. Polyps were either removed by conventional polypectomy or EMR. We excluded studies with data on polyps < 1 cm. We also excluded studies where polyps were resected exclusively by endoscopic submucosal dissection (ESD). All articles were downloaded into Endnote 7.0, a bibliographic database manager. Duplicate citations were removed.

Data extraction and quality assessment

Two authors (F.K. and M.A.K.) independently assessed the eligibility of included studies and extracted data using data extraction forms. The data extracted by individual authors were compared and any discrepancies were discussed with a third reviewer (C.W.H.) and agreement reached by consensus. Extracted data included year and country of publication, patient demographics, numbers of patients and polyps with DPPB in each group, rate of DPPB in patients on and not on anticoagulants/antiplatelet drugs, numbers/proportions of polyps in the proximal and distal colon, and rates of perforation, and post-polypectomy syndrome in each group. We used Cochrane tool for assessing risk of bias for RCTs to assess the quality of included studies. Two authors (F.K. and H.M.) independently performed quality assessment and any disagreement was discussed with a third reviewer (C.W.H.).

Data synthesis and statistical analysis

The primary outcomes of interest were DPPB with polyps between 1 cm and 1.9 cm in size and polyps ≥ 2 cm in size. Secondary outcomes of interest were post-polypectomy bleeding with all polyps ≥ 1 cm in size, proximal polyps, distal polyps, anticoagulant/antiplatelet drug use, perforation and post-polypectomy syndrome. We performed pre-determined subgroup analyses based on location of polyps (proximal *vs* distal) and anticoagulation/antiplatelet vs no anticoagulation/antiplatelet use. Sensitivity analyses were performed based on inclusion or exclusion of pedunculated polyps in studies or if any other hemostatic method was used in the no hemoclip group such as cauterization of the cut surface of the polyp. Data were analyzed using a fixed effect model and reported as pooled risk ratio (RR) with 95 % confidence interval (CI). A *P* value of < 0.1 for Cochran Q test or an I^2 value > 50 % indicated significant heterogeneity. The statistical analysis was performed using Review Manager (RevMan, version 5.3 for Windows; The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark, 2014).

Results

Search strategy yield and quality assessment

The search strategy produced 1245 articles, 303 of which were removed as duplicates (▶ **Fig. 1**). From the remaining 942 articles, 929 were removed after title and abstract review. An additional five relevant articles were identified by backward snowballing. Full texts of 18 articles were reviewed and nine, comprising 4550 patients, were included in the final analysis [13–15, 17–22]. Eight were full publications [13–15, 18–22] and one was only available as an abstract [17]. The characteristics of included studies are summarized in ▶ **Table 1** and ▶ **Table 2**. A total of 3764 polyps were included in analysis – 1917 with HC placement and 1847 without. Only three studies reported data on proximal and distal location of polyps [13–15]; 875 polyps were in the proximal colon and 402 were distal.

Meta-analysis

Polyps ≥ 2 cm in size

Overall DPPB

There were five studies with 1492 polypectomies [13–15, 18, 19]; 739 polyps received HC placement and 753 did not. Rates of DPPB were 4 % and 7 %, respectively; pooled RR (95 % CI) 0.55 (0.36, 0.86), Cochran Q test $P = 0.54$, $I^2 = 0$ % (▶ **Fig. 2**). Sensitivity analysis performed after excluding two studies that had included pedunculated polyps continued to show benefit of HC placement in prevention of DPPB: pooled RR (95 %CI) 0.51 (0.32, 0.82), $I^2 = 6$ % and this benefit reached statistical significance. Of the two excluded studies, one only included pedunculated polyps [19] and the other included both pedunculated and sessile polyps [13].

DPPB with proximal polyps

Three studies reported rates of DPPB with proximal polyps ≥ 2 cm in size [13–15]; 423 polyps received HC placement and 452 did not. Rates of DPPB were 4 % and 10 %, respectively; pooled RR (95 % CI) 0.41 (0.24, 0.70), Cochran Q test P = 0.22, $I^2 = 33$ % (▶ **Fig. 3a**). Sensitivity analysis excluding one study with both pedunculated and sessile polyps [13] showed similar results; pooled RR (95 % CI) 0.35 (0.19, 0.62), $I^2 = 0$ %.

DPPB with distal polyps

Three studies reported rates of DPPB with distal polyps ≥ 2 cm in size [13–15]. 208 polyps received HC placement and 194 did not. Rates of DPPB was 4 % and 3 %, respectively; pooled RR (95 % CI) 1.23 (0.45, 3.32), Cochran Q test P = 0.30, $I^2 = 17$ % (▶ **Fig. 3b**). On sensitivity analysis after excluding one study with both pedunculated and sessile polyps [13], pooled RR (95 % CI) was 1.52 (0.51, 4.54), $I^2 = 36$ %.

DPPB according to anticoagulant/antiplatelet drug use

We found evidence of benefit of HC placement in prevention of DPPB in the setting of anticoagulat/antiplatelet drug use (pooled RR (95 % CI) 0.50 (0.25, 0.99), $I^2 = 0$ %) as well as no anticoagulant / antiplatelet drug use (pooled RR (95 % CI) 0.42

▶ **Table 1** Characteristics of included studies.

Study, year	Country	Number of patients	Males	Inclusion criteria	Exclusion criteria	Quality assessment
Albeniz et al, 2019	Spain	235	158	Adults > 18 years of age scheduled for EMR of one large (≥ 2 cm) nonpedunculated colorectal lesions with substantial DB risk (GSEED-RE score ≥ 6). Patients with only one large polyp.	Simultaneous presence of more than one large (≥ 20 mm) polyp, lesions resected by ESD, incomplete EMR, lesions displaying an invasive pattern, previous endoscopic attempts, suspected damage in the muscularis propria, use of adrenaline in the injection solution and history of a hematological disease or coagulation disorder.	Low risk of selection, performance, detection, attrition and reporting bias.
Pohl et al, 2019	Multicenter	919	547	All patients between 18–89 years of age with a 20 mm non-pedunculated polyp	Patients with inflammatory bowel disease, poor health (American Society of Anesthesiologists class IV), coagulopathy (INR 1.5, platelets < 50), or a poor bowel preparation quality) Polyps with a pedunculated (Paris Ip), subpedunculated (Paris Isp), or ulcerated (Paris III) morphology and those with proven invasive cancer	Low risk of selection, performance, detection, attrition and reporting bias.
Feagins et al, 2019	USA	1050	1015	Patients with a polyp at least 1 cm in size that the endoscopist planned to remove	When immediate bleeding or concern for perforation occurred during the polypectomy that required treatment with a hemoclip (at the discretion of the endoscopist), those patients were excluded.	Low risk of selection, performance, detection, attrition and reporting bias.
Quintanilla et al, 2012	Spain	98	NR	Patients with one or more pedunculated polyps, the heads of which measured more than 1 cm (regardless of the stalk thickness and length). No hemostatic alterations at the time of endoscopy (confirmed by the usual blood tests taken before the procedure).	Patients younger than 18 years of age, platelet count < 50,000, INR > 1.5, patients who refused to give informed consent.	Low risk of selection, detection, attrition and reporting bias, unclear risk of performance bias, high risk of reporting bias.
Zhang et al, 2016	China	348	219	Patients with colorectal lesions > 1 cm to < 4 cm	Patients with blood disease, coagulation dysfunction, history of colorectal surgical resection, taking an anticoagulant, with lesions displaying an invasive pattern and those recurrent or residual tumors	Low risk of selection, detection, attrition and reporting bias. Unclear risk of performance bias.
Matsumoto et al, 2016	Japan	1499	1047	patients with colonic polyps < 2 cm and > 20 years of age. All of the patients had already received colonoscopy and were known to have polyps to resect.	Patients with a bleeding tendency (bleeding time > 5 min, platelet count < 50,000), or patients with serious complications (such as liver cirrhosis and renal disease requiring hemodialysis).	Low risk of selection, performance, detection, attrition and reporting bias.
Mori et al	Japan	62	NR	Polyps between 10 and 20 mm.	Polyps < 10 mm and > 20 mm.	Low risk of selection, attrition and reporting bias. High risk of performance bias, unclear risk of detection bias.
Dokoshi et al, 2015	Japan	156	108	NR	NR	Low risk of selection, performance, detection, attrition and reporting bias.
Ji et al, 2017		183	NR	patients who had pedunculated colorectal polyps, with heads > 10 mm and stalks > 5 mm in diameter	NR	Incomplete data for quality assessment

EMR, endoscopic mucosal resection; DB, delayed bleeding; ESD, endoscopic submucosal resection; GSEED-RE, Endoscopic Resection Group of the Spanish Society of Endoscopy; IV, intravenous; INR, international normalized ratio; NR, not reported

▶ **Table 2** Data on outcomes of interest.

Study	Groups	Number of patients in each group	Number of polyps	DPPB	DPPB from proximal polyps	DPPB from distal polyps	DPPB with Anticoagulant/ antiplatelet use	DPPB with no Anticoagulant/ antiplatelet use	Perforation	Post-polypectomy syndrome
Polyps > 2 cm										
Albeniz et al, 2019	HC	119	119	6	4/90	2/29	5/50	1/69	1	3
	No HC	116	116	14	11/88	3/28	8/34	6/82	1	0
Pohl et al, 2019	HC	455	490	16	10/305	6/150	6/116	10/339	3	1
	No HC	464	499	33	31/323	2/141	14/152	19/312	6	1
Feagins et al, 2019	HC	NR	101	4	3/28	0/29	NR	NR	0	NR
	No HC		121	6	3/41	1/25			0	
Quintanilla et al, 2012	HC	NR	21	1	NR	NR	NR	NR	1	NR
	No HC		11	0					0	
Dokoshi et al, 2015	HC	NR	8	2	NR	NR	NR	NR	NR	NR
	No HC		6	0						
Polyps 1–1.9 cm										
Quintinilla et al, 2012	HC	NR	45	0	NR	NR	NR	NR	0	NR
	No HC		28	0					0	
Mori et al, 2015	HC	NR	73	2	NR	NR	NR	NR	0	NR
	No HC		75	0					0	
Matsumoto et al, 2016	HC	NR	208	7	NR	NR	NR	NR	NR	NR
	No HC		131	5						
Feagins et al, 2019	HC	NR	579	13	NR	NR	NR	NR	0	NR
	No HC		585	13					0	

DPPB, delayed post-polypectomy bleeding; HC, hemoclip; NR, not reported

(0.21, 0.85), $I^2 = 0\%$). However, only two studies [14, 15] reported data on this outcome.

Perforation

There were four studies [13–15, 19] with 1478 polyps (731 with HC placement and 747 without) that reported rates of perforation. These were 0.7% and 0.9%, respectively; pooled RR (95% CI) 0.67(0.22, 2.05), Cochran Q test P = 0.76, $I^2 = 0\%$.

Post-polypectomy syndrome

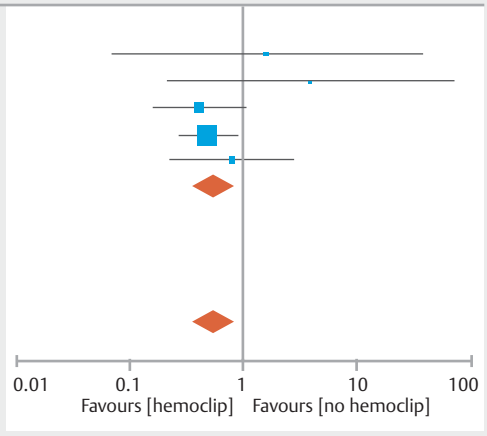
There were two studies [14, 15] with 1224 polyps (609 with HC placement and 615 without). Rates of post-polypectomy syndrome were 0.6% and 0.2%, respectively; pooled RR (95% CI) 2.98(0.47, 18.99), $I^2 = 0\%$.

Polyps 1–1.9 cm in size

DPPB

There were four studies with 1724 polyps [13, 19–21], 905 with HC placement and 819 without. Rates of DPPB were 2.4% and 2.2%, respectively; pooled RR (95% CI) 1.07 (0.59, 1.97), Cochran Q test $P = 0.56$, $I^2 = 0\%$ (▶ **Fig. 4a**). No studies compared rates of DPPB from removal of proximal and distal polyps with or without HC placement. One study [21] employed cauterization of the cut surface of the polyp after initial resection in patients who did not have HC placement. Sensitivity analysis after excluding this study showed similar results; pooled RR (95% CI) 0.97(0.52, 1.82), $I^2 = 0\%$. Since all studies included both pedunculated and sessile polyps, a sensitivity analysis based on morphology of polyps could not be performed.

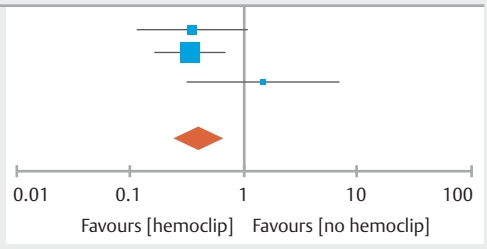
Study or subgroup	Hemoclip Events	Hemoclip Total	No hemoclip Events	No hemoclip Total	Weight	Risk ratio M-H, fixed, 95% CI	Year
1.1.1 RCTs							
Quintanilla et al, 2012	1	21	0	11	1.2%	1.64 [0.07, 37.15]	2012
Dokoshi et al, 2015	2	8	0	6	1.1%	3.89 [0.22, 68.67]	2015
Albeniz et al, 2019	6	119	14	116	26.5%	0.42 [0.17, 1.05]	2019
Pohl et al, 2019	16	490	33	499	61.1%	0.49 [0.28, 0.89]	2019
Feagins et al, 2019	4	101	6	121	10.2%	0.80 [0.23, 2.75]	2019
Subtotal (95% CI)		**739**		**753**	**100.0%**	**0.55 [0.36, 0.86]**	
Total events	29		53				
Heterogeneity: Chi² = 3.08, df = 4 (*P* = 0.54); I² = 0%							
Test for overall effect: Z = 2.64 (*P* = 0.008)							
Total (95% CI)		**739**		**753**	**100.0%**	**0.55 [0.36, 0.86]**	
Total events	29		53				
Heterogeneity: Chi² = 3.08, df = 4 (*P* = 0.54); I² = 0%							
Test for overall effect: Z = 2.64 (*P* = 0.008)							
Test for subgroup differences: Not applicable							



▶ **Fig. 2** Forest plot to compare DPPB in polyps ≥ 2 cm in size with prophylactic HC vs no HC.

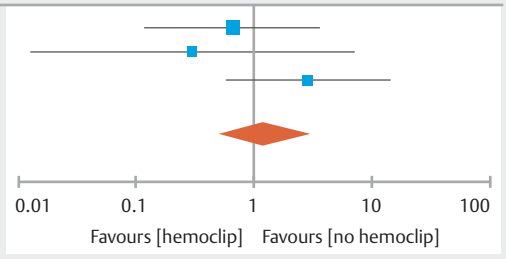
Study or subgroup	Hemoclip Events	Hemoclip Total	No hemoclip Events	No hemoclip Total	Weight	Risk ratio M-H, fixed, 95% CI	Year
Albeniz et al, 2019	4	90	11	88	25.5%	0.36 [0.12, 1.07]	2019
Pohl et al, 2019	10	305	31	323	69.0%	0.34 [0.17, 0.68]	2019
Feagins et al, 2019	3	28	3	41	5.6%	1.46 [0.32, 6.74]	2019
Total (95% CI)		**423**		**452**	**100.0%**	**0.41 [0.24, 0.70]**	
Total events	17		45				
Heterogeneity: Chi² = 3.00, df = 2 (*P* = 0.22); I² = 33%							
Test for overall effect: Z = 3.28 (*P* = 0.001)							

a



Study or subgroup	Hemoclip Events	Hemoclip Total	No hemoclip Events	No hemoclip Total	Weight	Risk ratio M-H, fixed, 95% CI
Albeniz et al, 2019	2	29	3	28	45.4%	0.64 [0.12, 3.57]
Feagins et al, 2019	0	29	1	25	23.9%	0.29 [0.01, 6.79]
Pohl et al, 2019	6	150	2	141	30.7%	2.82 [0.58, 13.74]
Total (95% CI)		**208**		**194**	**100.0%**	**1.23 [0.45, 3.32]**
Total events	8		6			
Heterogeneity: Chi² = 2.41, df = 2 (*P* = 0.30); I² = 17%						
Test for overall effect: Z = 0.40 (*P* = 0.69)						

b



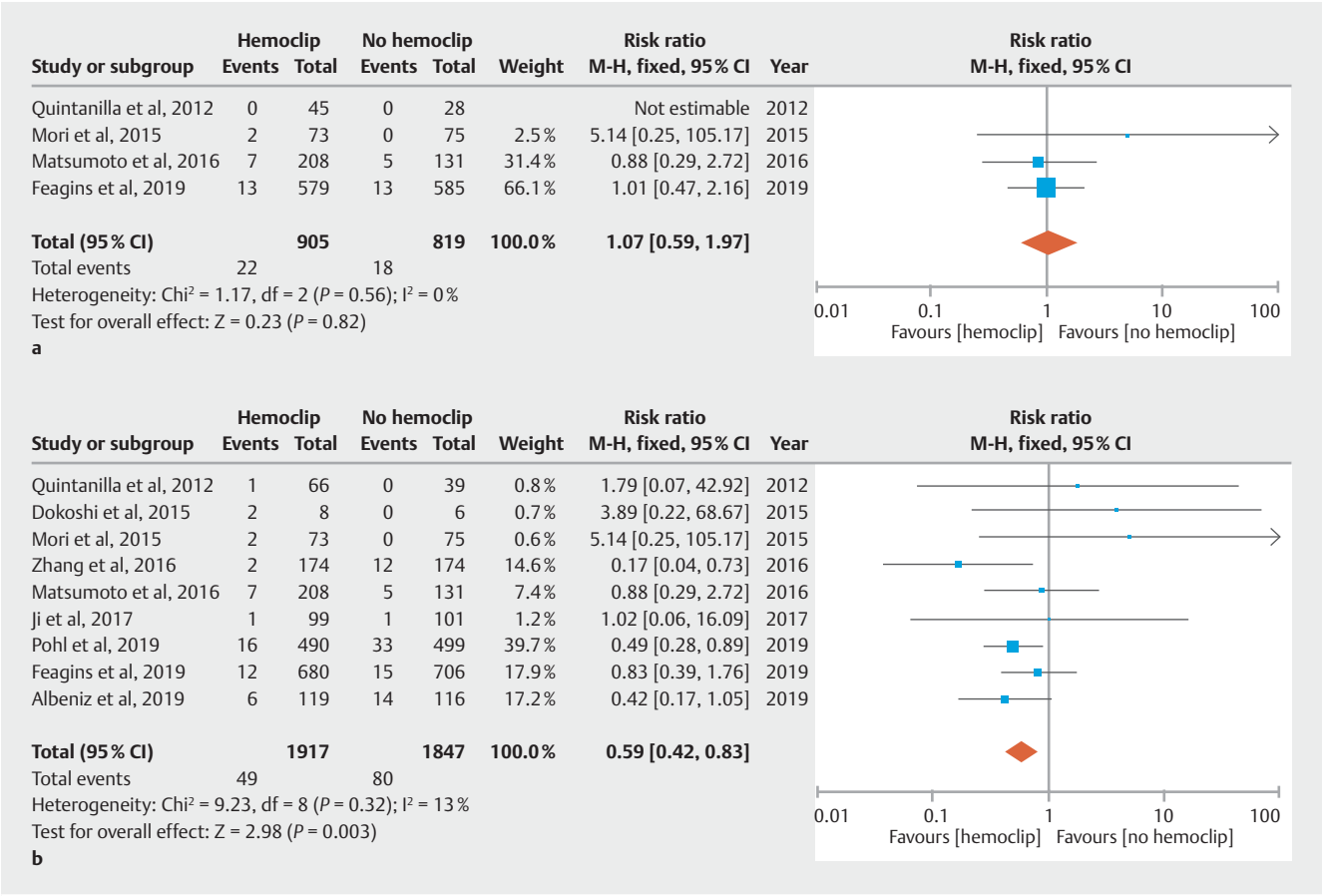
▶ **Fig. 3** Forest plot to compare DPPB in proximal (**a**) and distal (**b**) colonic polyps ≥ 2 cm in size with prophylactic HC vs no HC.

Perforation

There were three studies with 1660 polyps (826 with HC placement and 834 without). Rates of perforation were 0.1% and 0.1%, respectively; pooled RR (95% CI) 1.00 (0.06, 15.86).

All polyps ≥ 1 cm in size

There were nine studies with 3764 polyps (1917 with HC placement and 1847 without). Rates of DPPB were 2.5% and 4.3%, respectively; pooled RR (95% CI) 0.59 (0.42, 0.83), Cochran Q test $P = 0.32$, $I^2 = 13\%$ (▶ **Fig. 4b**). We performed sensitivity analysis by excluding two studies that had only included polyps > 2 cm in size [14, 15]. This analysis showed no significant benefit of HC use in prevention of DPPB; pooled RR (95% CI) 0.75 (0.45, 1.23), Cochran Q test $P = 0.30$, $I^2 = 17\%$. Sensitivity analysis by further excluding one study where a subset of polyps were resected by ESD [22] did not change the results; pooled RR (95% CI) 1.04 (0.60, 1.82), $I^2 = 0\%$.



▶ **Fig. 4** Forest plot to compare DPPB in polyps 1 to 1.9 cm (**a**) and any polyp ≥ 1 cm (**b**) in size with prophylactic HC vs no HC.

Discussion

For cost-effective and safe practice, careful patient selection is necessary for prophylactic HC placement. Currently there is no standardized practice regarding the prophylactic use of HCs; accordingly, endoscopists exercise their clinical judgement. Our meta-analysis indicates that the benefit of HC placement for the prevention of DPPB is limited to large polyps (≥ 2 cm) located in the proximal colon.

Two previous meta-analyses [23, 24] showed conflicting results while evaluating the role of HC placement in prevention of DPPB. Forbes et al [23] also included only RCTs but showed no benefit of HCs in prevention of DPPB; pooled RR (95% CI) 0.86 (0.55, 1.36). However, most of the polyps in this study were < 1 cm. A subgroup analysis of 122 polyps that were ≥ 2 cm in size also showed no benefit of HC placement [23]. Their conclusions differed from ours, probably due to difference in sample sizes. Our analysis included 1492 polyps that were ≥ 2 cm in size.

Ayoub et al [23] included both RCTs and observational studies but showed benefit of HC placement in prevention of DPPB for polyps ≥ 2 cm; pooled OR (95% CI) 0.25 (0.12, 0.51) [24]. They included 1701 polyps that were ≥ 2 cm in size. A subgroup analysis for proximal colon polyps could not be performed as only one included study reported the relevant data. A subgroup analysis including only RCTs showed no benefit of HC placement in prevention of DPPB: pooled OR (95% CI) 0.77(0.36, 1.65) but this analysis included polyps of any size.

Our subgroup analyses based on location of polyps that were ≥ 2 cm in size showed benefit of HC placement for proximal – but not distal – polyps and that this benefit was statistically significant. This is consistent with previously published data suggesting that polyps in the proximal colon carry a greater risk of DPPB [9]. Although we found no statistically significant benefit of HC placement for distal colon polyps that were ≥ 2 cm, this should be interpreted carefully. First, only three studies with 402 polyps could be included. Second, there was no subgroup analysis based on anticoagulant / antiplatelet drug use, which is a risk factor for DPPB. Therefore, HC placement should still be considered after removal of distal colon polyps that were ≥ 2 cm in patients who were recently on anticoagulants and/or antiplatelet drugs.

We found no statistically significant benefit of HC placement in prevention of DPPB for polyps 1 to 1.9 cm in size. This is a new finding that was not addressed in previous meta-analyses. This is a clinically important finding as endoscopists may be relatively unsure of the value in HC placement for these relatively smaller polyps. However, one important limitation of this analysis is that no studies evaluated the effect of HC placement on rates of DPPB for proximal polyps 1–1.9 cm in size or in the setting of

anticoagulant/antiplatelet drug use. However, whether HCs should be used routinely for proximal colon polyps 1 to 1.9 cm in size in patients on anticoagulants and/or antiplatelet drugs remains unclear and needs further investigation.

Finally, we performed a separate analysis including all polyps ≥ 1 cm to capture those studies that also evaluated the usefulness of HCs for polyps ≥ 1 cm and did not make subgroups for polyps 1 to 1.9 cm and ≥ 2 cm. Although this initially showed a statistically significant benefit of HC placement, this was not maintained after the exclusion of two studies in which all polyps were ≥ 2 cm in size.

Strengths of our meta-analysis are its restriction to RCTs and the low levels of heterogeneity for all outcomes of interest. RCTs represent the highest level of evidence and it has been proposed that they should not be included with observational studies [25]. Lack of randomization, necessary for the control of measured and unmeasured confounding and confounding by indication, can seriously affect the validation of results from observational studies [26]. We performed several pre-determined subgroup analyses to identify subgroups most likely to benefit from HC placement.

There are also some inevitable limitations of this meta-analysis. Although use of anticoagulants and /or antiplatelet drugs is a known risk factor for DPPB, only two studies reported data on the usefulness of HCs in this setting. Therefore, firm conclusions cannot be made regarding the role of HCs. Albeniz et al reported rates of DPPB of 1.5 % and 9.1 %, respectively, in their complete closure and partial closure groups [14]. Because not all mucosal defects can be closed completely with HCs, their routine use in this setting may still be useful for the prevention of DPPB. Another study reported rates of DPPB of 2.4 % and 3.1 % in complete closure and partial closure groups, respectively [15]. More studies are required to evaluate this outcome.

None of the included studies evaluated risk of DPPB in the setting of anticoagulant/antiplatelet drug use, or for proximal and distal location of polyps that were 1 to 1.9 cm in size. Since several studies included both pedunculated and sessile polyps, we could not perform sensitivity analysis confined to sessile polyps for all outcomes of interest. This may have clinical relevance because the means whereby hemoclips might prevent DPPB may differ for pedunculated and sessile polyps. For sessile polyps, the aim of using HCs is to close the mucosal defect; for pedunculated polyps, it is to occlude vasculature in the polyp stalk. However, several studies suggest that polyp morphology does not influence DPPB [27–29].

Conclusion

In conclusion, use of HCs may only be beneficial for patients having resection of polyps ≥ 2 cm in size that are located in the proximal colon. For efficient and cost-effective practice, restricting their use to such patients – who are most likely to derive benefit – is recommended. More widespread use of HCs cannot be justified based on current evidence.

Competing interests

The authors declare that they have no conflict of interest.

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