



ORIGINAL ARTICLE

# Endoscopic management of delayed bleeding after polypectomy of small colorectal polyps: two or more clips may be safe

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## Abstract

**Background:** The resection of small colorectal polyps ( $\leq 10$  mm) is routine for endoscopists. However, the management of one of its main complications, namely delayed (within 14 days) postpolypectomy bleeding (DPPB), has not been clearly demonstrated. We aimed to assess the role of colonoscopy in the management of DPPB from small colorectal polyps and identify the associated factors for initial hemostatic success.

**Methods:** We conducted a retrospective study of 69 patients who developed DPPB after the removal of colorectal polyps of  $\leq 10$  mm and underwent hemostatic colonoscopy at the Sixth Affiliated Hospital of Sun Yat-sen University (Guangzhou, China) between April 2013 and June 2021. Demographics, clinical variables, and colonoscopic features were collected independently. We applied univariate and multivariate analyses to assess factors associated with initial hemostatic success.

**Results:** General colonoscopy without oral bowel preparation was successfully performed in all the patients, with a median duration of 23.9 (12.5–37.9) minutes. Among 69 patients, 62 (89.9%) achieved hemostasis after initial hemostatic colonoscopy and 7 (10.1%) rebled  $2.7 \pm 1.1$  days after initial colonoscopic hemostasis and had rebleeding successfully controlled by one additional colonoscopy. No colonoscopy-related adverse events occurred. Multivariate analysis showed that management with at least two clips was the only independent prognostic factor for initial hemostatic success (odds ratio, 0.17; 95% confidence interval, 0.03–0.91;  $P = 0.04$ ). All the patients who had at least two clips placed at the initial hemostatic colonoscopy required no further hemostatic intervention.

**Conclusions:** Colonoscopy is a safe, effective, and not too time-consuming approach for the management of patients with DPPB of small colorectal polyps and management with the placement of at least two hemoclips may be beneficial.

**Key words:** colonoscopy; gastrointestinal bleeding; polypectomy; clip; complication

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## Introduction

Colonoscopic polypectomy is well established to reduce colorectal-cancer incidence and cancer-related mortality [1]. Over 90% of polyps detected during screening colonoscopy are small lesions ( $\leq 10$  mm) and therefore endoscopic resection of those polyps has become routine for every endoscopist [2, 3]. Colonoscopic polypectomy is generally safe, but not risk-free, with postpolypectomy bleeding (PPB) being the most frequent complication. Delayed PPB (DPPB) typically occurs 2–7 days following polypectomy and its incidence is commonly reported to be 0.2%–2.2% [4, 5]. Several studies have elucidated the polyp size as a major risk factor for DPPB [6, 7]. In a study including 15,553 polypectomies, Zhang et al. [8] found that a polyp size of  $>10$  mm was independently associated with DPPB (odds ratio [OR], 4.6; 95% confidence interval [CI], 2.9–7.2). The exact incidence of DPPB for small colorectal polyps of  $\leq 10$  mm is lacking. Makino et al. [9] reported an incidence of DPPB to be 1.2% (2/172) in patients undergoing polypectomies for small colorectal polyps without discontinuation of antithrombotic drugs. Since the total amount is large, the absolute number of DPPBs from colorectal polyps of  $\leq 10$  mm is substantial and should not be negligible in the daily clinic.

Most studies in DPPB have focused on demonstrating the risk factors and prophylactic interventions, while little research has discussed the management and outcomes of DPPB. In a retrospective study by Rodríguez et al. [10], 394 patients underwent colonoscopy for DPPB, 344 (87.3%) had bleeding points identified, 290 (73.6%) received hemostatic treatment, and 39 (9.9%) rebled after the initial management. Notably, only 25.0% of polyps were small lesions in this cohort. Burgess et al. [11] also developed a management algorithm for DPPB of colorectal polyps of  $\geq 20$  mm. However, heterogeneity does exist between small and large colorectal polyps in polypectomy difficulty, methods, prophylactic therapies, and perioperative management, which may lead to differences in the characteristics and severity of DPPB. Few studies have addressed the endoscopic management of delayed bleeding after polypectomy of small colorectal polyps [12]. The purpose of our study was to assess the outcomes following endoscopic management of DPPB from colorectal polyps of  $\leq 10$  mm and to evaluate the risk factors for rebleeding. Secondarily, we aimed to assess the management of rebleeding.

## Patients and methods

### Study design and patients

This was a retrospective study conducted at the Sixth Affiliated Hospital of Sun Yat-sen University (Guangzhou, China) and approved by the Institutional Review Board of the institution (No. 2020ZSLY-251). Patients who underwent endoscopic management for DPPB from colorectal polyps of  $\leq 10$  mm between April 2013 and June 2021 were included. We excluded patients whose polypectomy was performed at other hospitals.

DPPB was defined as any rectal bleeding developing within 14 days of polypectomy, with the patient manifesting hematochezia, melena, or acute blood-loss anemia [13]. A polyp was identified responsible for bleeding if active bleeding or adherent clot was presented at the polyp scar or if only one polyp was resected [14]. If the requirements were not fulfilled, the largest polyp resected was analysed as being responsible for the bleeding [10]. Rebleeding was defined as recurrent rectal bleeding that occurred after the initial successful colonoscopic hemostasis and needed another intervention. Patients were classified into two groups according to the presence of rebleeding.

We retrospectively reviewed medical charts and endoscopy records. We abstracted baseline data, including age, gender, body mass index (BMI), co-morbidity (including diabetes, hypertension, and cerebrovascular disease), use of anticoagulants and antiplatelets, and laboratory findings before initial hemostatic colonoscopy. We retrieved polyp information from the index colonoscopy, including date of polypectomy, number of polyps, characteristics of the index or bleeding polyp (such as the size, morphology, location, and histology), methods of polypectomy, intraprocedural bleeding, and use of hemoclips. We reviewed the information on colonoscopic hemostasis, such as the date, treatment place (inpatient or outpatient), hemostasis methods, and clinical outcomes (14-day rebleeding, complications, and mortality). We also recorded the status of the polyp scar, including active bleeding, adherent clot, and pigment spot (Figure 1). Regarding the rebleeding episode, we recorded the date of the colonoscopic hemostasis, location and status of the bleeding point, hemostasis methods, and clinical outcomes. Success of colonoscopic hemostasis was defined as no bleeding for 14 days after endoscopic therapy [15].

### Statistical analysis

Depending on normality, continuous variables were reported as mean  $\pm$  standard deviation or median (interquartile range [IQR]) and compared using the Student's *t*-test or Wilcoxon rank-sum test. Categorical variables were reported as numbers (percentage) and compared using the Chi-squared test or Fisher's exact test. We performed multivariate regression analyses to identify risk factors associated with rebleeding after initial endoscopic hemostasis. Firth's logistic regression was selected for the analysis of the binary outcome with a small sample size and variables with  $P \leq 0.10$  in the univariate analyses were included in the final model. All statistical analyses were performed using SPSS version 23 (SPSS Inc., Chicago, IL, USA) and SAS 9.4 (SAS Institute Inc., Cary, NC). A two-sided *P*-value of  $<0.05$  was considered significant.

## Results

### Demographics

Between April 2013 and June 2021, a total of 37,895 patients received polypectomy for small colorectal polyps of  $\leq 10$  mm. Of the 75,007 small polyps identified, 20,095 (26.8%) polyps were resected using cold polypectomy, while the others had hot polypectomy. DPPB occurred in 69 patients (0.2%) with 233 polyps (Figure 2). The median age of these 69 patients was 50.0 years and 75.4% of them were male. Only one patient had a low platelet count ( $89 \times 10^3/\text{mm}^3$ ) and three had a slightly elevated international normalized ratio (INR). Thirty-seven of the resected polyps (53.6%) were in the left colon (from splenic flexure to rectum). All but one of the polyps (98.6%) were resected using electrocautery. Submucosal injection with normal saline solution was performed in 36.2% of the patients. Epinephrine was not used in the index colonoscopy. Prophylactic hemoclips were placed in 49.3% of the patients, with a median number of 0 (0–1) (Table 1).

### Management of DPPB

DPPB occurred at a median of 3.0 (IQR, 2.0–6.0) days after polypectomy. Forty-eight (69.6%) patients underwent inpatient colonoscopy for hemostasis and the rest underwent outpatient colonoscopy, with a median duration of 23.9 minutes (Table 1).

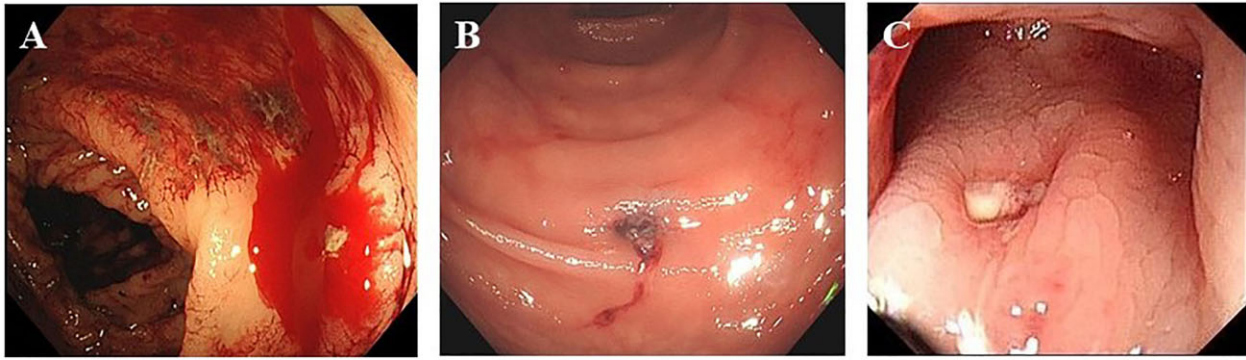


Figure 1. Status of the polyp scar. (A) Active bleeding. (B) Adherent clot. (C) Pigment spot.

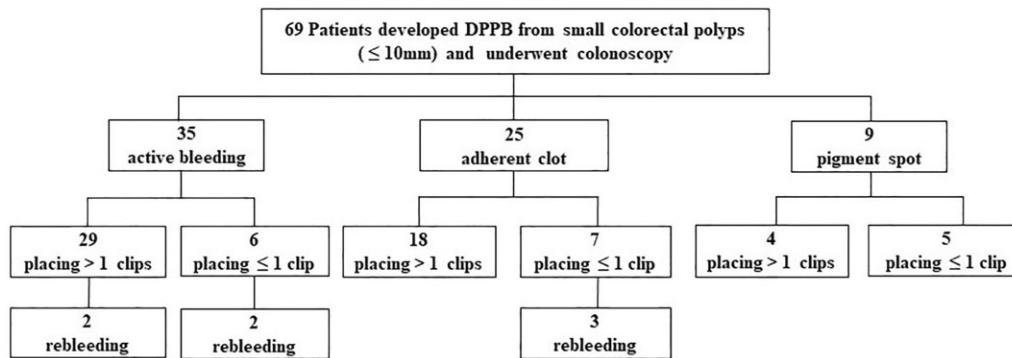


Figure 2. Flowchart of patients enrolled in this study

All patients received general colonoscopy, requiring no bowel preparation. Regarding the status of the polyp scar, 35 (50.7%) patients presented with active bleeding, 25 (36.2%) presented with adherent clot, and the other 9 (13.0%) presented with pigment spot. All but three patients (95.7%) received intervention during colonoscopy. Hemoclips alone (60/69, 87.0%) or combined with other therapy (three with local injection of adrenaline, one with thermal probe, and one with nylon string) were the most commonly used modalities. Forty-three patients (62.3%) began a liquid diet after colonoscopy and the others fasted for  $\geq 24$  hours. Successful intraprocedural hemostasis was achieved in all 69 patients and successful initial endoscopic hemostasis achieved in 62 (89.9%). There were no complications related to the endoscopy.

According to the outcomes of the initial endoscopic management, patients were classified into rebleeding and non-rebleeding groups (Table 1). They were comparable in most demographic characteristics, laboratory findings, and polyp features. The rebleeding rates were no different between patients undergoing inpatient or outpatient hemostatic colonoscopy, nor in patients who did or did not fast for  $\geq 24$  hours.

The rebleeding-positive group tended to be younger (42 vs 52 years,  $P=0.074$ ) and had a larger proportion of 6- to 10-mm polyps (100.0% vs 54.8%,  $P=0.057$ ), although it was not statistically significant. The univariate analysis demonstrated a statistically significant association between hemostatic success and management with at least two clips ( $P=0.015$ ). Further multivariate analysis confirmed management with at least two clips as an independent prognostic factor for hemostatic success (OR = 0.173, 95% CI: 0.033–0.913,  $P=0.039$ ).

### Management of rebleeding

Seven patients rebled at a mean of 2.7 days after initial colonoscopic hemostasis. All of them achieved successful hemostasis by only one additional colonoscopy, with no complications. Two patients who had at least two clips placed at the initial hemostatic colonoscopy presented with pigment spot at the second session requiring no intervention (Table 2). Of the other five patients who had  $\leq 1$  clip placed, three presented with active bleeding at the second session. They achieved successful hemostasis after having at least two clips placed.

Overall, all 51 patients (51/69, 73.9%) who had at least two clips placed at the initial hemostatic colonoscopy required no further hemostatic intervention.

### Discussion

There is no guideline for the management of DPPB at present; only a few studies have summarized the experience [10, 15]. These studies contained a majority of, or entirely, large colorectal polyps, which means that those findings may not be simply extrapolated to small polyps. In this retrospective study, we assessed the safety and efficacy of prompt colonoscopy for DPPB of colorectal polyps of  $\leq 10$  mm. General colonoscopy without oral bowel preparation was successfully performed in all the patients, with a median duration of 23.9 minutes. After hemostatic colonoscopy, 62.3% of patients began a liquid diet. The successful rate of initial colonoscopic hemostasis was 89.9% and all the rebleeding was successfully controlled by one additional colonoscopy. No adverse events occurred. Management

**Table 1.** Baseline characteristics of 69 patients in non-rebleeding and rebleeding groups

Variable	Total (n = 69)	Non-rebleeding (n = 62)	Rebleeding (n = 7)	Univariate P-value	Multivariate	
					OR (95% CI)	P-value
Age, years, median (IQR)	50 (38.5–63.5)	52 (40.0–64.0)	42 (23.0–54.0)	0.07	0.96 (0.91–1.02)	0.20
Male, n (%)	52 (75.4)	46 (74.2)	6 (85.7)	0.84		
Co-morbidity, n (%)	15 (21.7)	13 (21.0)	2 (28.6)	1.00		
BMI, kg/m <sup>2</sup> , mean ± SE	23.3 ± 4.1	23.3 ± 3.8	23.2 ± 6.3	0.98		
Antiplatelet and/or anticoagulant therapy, n (%)	3 (4.3)	3 (4.8)	0 (0.0)	1.00		
INR, median (IQR)	1.01 (0.97–1.07)	1.01 (0.96–1.07)	1.07 (0.97–1.14)	0.50		
Platelet count, ×10 <sup>3</sup> /mm <sup>3</sup> , mean ± SE	228.9 ± 59.4	230.2 ± 62.2	219.6 ± 34.1	0.66		
Quantity of polyps, n (%)				0.42		
≤3	44 (63.8)	41 (66.1)	3 (42.9)			
>3	25 (36.2)	21 (33.9)	4 (57.1)			
Size of responsible polyp, n (%)				0.06		
≤5 mm	28 (40.6)	28 (45.2)	0 (0.0)		0.10 (0.01–1.92)	0.13
>5 mm	41 (59.4)	34 (54.8)	7 (100.0)		Reference	
Responsible polyp						
Morphology of responsible polyp, n (%)				1.00		
Pedunculated	4 (5.8)	4 (6.5)	0 (0.0)			
Non-pedunculated	65 (94.2)	58 (93.5)	7 (100.0)			
Location of responsible polyp, n (%)				0.55		
Right colon	32 (46.4)	30 (48.4)	2 (28.6)			
Left colon	37 (53.6)	32 (51.6)	5 (71.4)			
Usage of cautery, n (%)				1.00		
Cold polypectomy	1 (1.4)	1 (1.6)	0 (0)			
Hot polypectomy	68 (98.6)	61 (98.4)	7 (100)			
Submucosal injection, n (%)	25 (36.2)	21 (33.9)	4 (57.1)	0.25		
Prophylactic hemoclip, n (%)	34 (49.3)	30 (48.4)	4 (57.1)	0.71		
Number of clips, median (IQR)	0 (0–1)	0 (0–1)	0 (0–1)	0.91		
Intraprocedural bleeding, n (%)	1 (1.4)	0 (0.0)	1 (14.3)	0.10		
Histology, n (%)				0.39		
Adenoma	44 (63.8)	38 (61.3)	6 (85.7)			
Inflammatory/hyperplastic	25 (36.2)	24 (38.7)	1 (14.3)			
Endoscopic hemostasis						
Time from polypectomy, days, median (IQR)	3.0 (2.0–6.0)	3.0 (2.0–6.0)	2.0 (1.0–4.0)	0.32		
Treatment place for hemostasis, n (%)				0.16		
Inpatient	48 (69.6)	41 (66.1)	7 (100.0)			
Outpatient	21 (30.4)	21 (33.9)	0 (0.0)			
Bleeding point, n (%)				0.74		
Active bleeding	35 (50.7)	31 (50.0)	4 (57.1)			
Visible vessel-adherent clot	25 (36.2)	22 (35.5)	3 (42.9)			
Pigment spot	9 (13.0)	9 (14.5)	0 (0.0)			
Management for bleeding, n (%)				0.02		
≤1 clip	18 (26.1)	13 (21.0)	5 (71.4)		Reference	
>1 clip	51 (73.9)	49 (79.0)	2 (28.6)		0.17 (0.03–0.91)	0.04
Duration of hemostasis, min, median (IQR)	23.9 (12.5–37.9)	24.1 (13.5–38.3)	12.8 (8.2–31.8)	0.23		
Fasting ≥24 h after hemostasis, n (%)	26 (37.7)	25 (40.3)	1 (14.3)	0.35		

BMI, body mass index; CI, confidence interval; INR, international normalized ratio; IQR, interquartile range; OR, odds ratio; SE, standard error.



**Table 2.** Management of patients with rebleeding

Case	Bleeding point	Management of bleeding	Time from initial hemostatic colonoscopy (days)	Rebleeding point	Clip in situ	Management of rebleeding
1	Active bleeding	2 clips	3	Pigment spot	√	×
2	Active bleeding	3 clips	2	Pigment spot	√	×
3	Active bleeding	1 clip with epinephrine injection	1	Active bleeding	√	2 clips
4	Active bleeding	APC	4	Adherent clot	–	×
5	Adherent clot	1 clip	3	Active bleeding	×	2 clips
6	Adherent clot	1 clip	2	Active bleeding	√	3 clips
7	Adherent clot	1 clip	4	Adherent clot	√	1 clip

APC, argon plasma coagulation.

with at least two clips was the only independent prognostic factor for initial hemostatic success. All the patients who had at least two clips placed at the initial hemostatic colonoscopy required no further intervention.

Colonoscopy is still the preferred method for managing DPPB for most endoscopists, though several researchers questioned that it was overused in DPPB. Sonnenberg [16] developed a decision-tree model and demonstrated that hemostatic colonoscopy for DPPB was beneficial in 22% of patients, corresponding to a number-needed-to-treat of 4.5 patients. The author concluded that it was beneficial to adopt hemostatic colonoscopy in a minority of patients and expectant management was a valid option for many patients. In a study including 15,285 colonoscopies, Derbyshire et al. [17] found that a drop in hemoglobin ( $\geq 2$  g/dL) and/or blood transfusion were independent predictors of a need for therapeutic intervention (endoscopic, radiological, or surgical). However, several noticeable issues prevent the clinical application for these research findings or predictive models. First, colonoscopy is a very safe procedure for PPB, with no related adverse events occurring in our and other studies. Besides, it only took a mean of 23.9 minutes in the present study. Second, previous studies often set the endoscopic intervention or identification of the active bleeding point as the primary outcome. But the identification of the bleeding status using colonoscopy is also important for both doctors and patients when making a decision on when to return to normal dietary and living conditions. Our study showed that no difference in the rebleeding rate existed between patients fasting for 24 hours or not after hemostatic colonoscopy, and no difference between patients undergoing inpatient or outpatient colonoscopy. Third, although current guidelines do not recommend unprepped colonoscopy in patients with acute lower gastrointestinal bleeding, few studies discussed the role of bowel preparation in the setting of DPPB [18, 19]. In fact, colonoscopy in DPPB is not as complicated as in undifferentiated lower gastrointestinal bleeding, as the possible bleeding site and cause are already known. Because colonoscopy was performed not long after polypectomy (last bowel preparation) and the existence of blood usually acts as a laxative, the large bowel could be devoid of too much stool and reasonably clean. Differently from Ma and Bourke's opinion [20], oral bowel preparation was not required in our institution, although a water pump was needed to rinse away contaminating material. A high percentage of stigmata was noted in hemostatic colonoscopy, with 50.7% of patients presenting with active bleeding, 36.2% presenting with adherent clot, and the other 13.0% presenting with pigment spots. This may be mainly attributable to timely colonoscopy (a

median of 3.0 days after polypectomy) and good bowel cleaning. Parra-Blanco et al. [21] advocated prompt colonoscopy not only for major bleeding, but also for frank episodes to prevent a "delayed treatment" that would undoubtedly increase the requirement for transfusion, hospitalization, and even surgery. To date, there is no study discussing patients' choice of prompt colonoscopy or expectant management for DPPB.

Hemoclipping is the preferred method of hemostasis for PPB. An electronic survey conducted in 2014 indicated that most gastroenterologists chose to use clips both to treat PPB and for prophylaxis [22]. In our study, 87.0% of patients received hemoclips alone or combined with other modalities, with an average number of 2.5 hemoclips. Initial colonoscopic hemostasis was achieved in 89.9% of the patients and all the rebleeding was successfully controlled by colonoscopy. In a study consisting of 42 patients with DPPB, Binmoeller et al. [23] found that hemoclips were useful in controlling active bleeding, with an average number of 2.9 hemoclips. Our study showed that the placing of at least two clips was the only independent prognostic factor for initial hemostatic success of DPPB of colorectal polyps of  $\leq 10$  mm. One possible explanation was that one clip might fall off or shift with bowel movement. In our study, in one of the four patients who had only one clip placed in the initial hemostatic colonoscopy, the clip had completely fallen off at the second session. Another possible explanation was that one clip could not ensure complete mechanical closure of the hemorrhaging vessels. Woo and Bechara [24] reported a case of DPPB after removal of colorectal polyps of  $\leq 10$  mm using a hot snare; a large visible vessel-adherent clot was found in the repeat colonoscopy. They placed two clips at the base and achieved hemostasis. Interestingly, our result was contrary to that of Lee et al. [15], who reported that a large number of hemoclips was an independent risk factor for failure of initial hemostasis in DPPB. The author explained that large numbers of hemoclips might indicate technical difficulty in the hemostatic procedure, which was associated with a significant risk of rebleeding. We believe that the opposite results should be largely attributed to the heterogeneity between small and large colorectal polyps. The mean size of the polyps was  $12.5 \pm 13.7$  mm in Lee et al.'s study [15]. It is worth noting that application of clips to thin-walled postpolypectomy ulcers should be done carefully, as related perforation has been reported.

Apart from hemoclips, other methods have been reported to be used for bleeding control. Sclerotherapy with adrenaline or forceps coagulation may be useful for intraprocedural hemostasis but not for rebleeding. As possibly increasing likelihood of perforation in thin-walled ulcers after polypectomy, they should not be the first choice for DPPB of small colorectal polyps [25]. An over-the-scope clip system has been demonstrated to have strong therapeutic

potential in upper gastrointestinal bleeding and has been used for the treatment of PPB after the failure of conventional treatment [26, 27]. This powerful method is less likely to be used for DPPB of small colorectal polyps. Hemostatic spray powder, as a new hemostatic agent, has already been shown to be effective and safe in treating postpolypectomy hemorrhage [28, 29]. The hemostatic powder also has a risk of sloughing off some time after treatment; a retrospective study of 21 Spanish centers reported higher rates of recurrent bleeding within the first 3 days [30]. Although more data are needed, researchers consider this a promising agent in DPPB [31].

A total of 49.3% of 69 patients with DPPB received prophylactic clip placement, with a median number of 0 (0–1). Our study showed that prophylactic clip placement was not associated with initial hemostatic success. Of the 75,007 small polyps identified, nearly 20.3% (15,249 polyps) were had prophylactic clips placed in the present study. However, using prophylactic hemoclips to prevent DPPB remains controversial. Several studies have demonstrated that the routine use of clips was unable to reduce DPPB [32–34]. But a recent meta-analysis showed a modest reduction in DPPB with prophylactic clip placement after polypectomy of colorectal polyps of  $\geq 20$  mm [35]. Further randomized trials are still needed to determine the role of prophylactic clips in the prevention of PPB.

The impact of age on DPPB is an interesting and still unclear issue. In a study including 30,881 single polypectomies, Rutter et al. [36] did not reveal any relationship between age and DPPB. Wu et al. [37] found that older age was a risk factor for DPPB in their univariate analysis, although not in the multivariate analysis. Park et al. [38] prospectively investigated the risk factors for DPPB in 8,175 polypectomies and found young age to be an independent risk factor in multivariate analysis. In our study, the univariate analysis demonstrated that younger age tended to be associated with rebleeding (42 vs 52,  $P = 0.074$ ). We agreed with Park et al.'s presumption [38] that younger patients might return to normal dietary and living conditions more urgently.

Our study had limitations, mainly due to the retrospective design and relatively small sample size. First, prospective, large-cohort studies are therefore warranted to validate our findings. Second, we could not compare the DPPB rate after various polypectomies for small colorectal polyps, as we did not assess the initial DPPB rates following different methods including cold biopsy forceps, cold snare polypectomy, hot biopsy forceps, hot snare, and endoscopic mucosal resection in all the patients. Third, the present study did not include patients with mild DPPB managed conservatively without colonoscopy. But this would not affect the validity of the conclusion that endoscopic management using at least two clips is a safe and effective method for DPPB of colorectal polyps of  $\leq 10$  mm. Finally, the study was conducted in a single tertiary hospital with a 24-hour emergency endoscopy service and caution should be exercised if our findings are being extrapolated.

In conclusion, management with prompt colonoscopy for DPPB of colorectal polyps of  $\leq 10$  mm is safe, effective, and not too time-consuming, and the placing of at least two clips may be beneficial.

## Authors' Contributions

Q.H.Z., J.C.H., and X.F.G. conceived of and designed the project. M.L.S., J.L., W.L., and J.W.Z. collected the data. X.A.Y., D.Z.L., J.X.D., and M.L.S. analysed and interpreted the data. X.F.G.,

X.A.Y., Q.H.Z., and J.C.H. drafted the manuscript. All authors read and approved the final manuscript.

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None.

## Conflict of Interest

None declared.

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