

ORIGINAL ARTICLE

# Risk factors for delayed hemorrhage after colonoscopic polypectomy: Polyp size and operative modality

Changqin Liu, Ruijin Wu, Xiaomin Sun, Chunhua Tao and Zhanju Liu 

Department of Gastroenterology and Hepatology, Shanghai Tenth People's Hospital of Tongji University, Shanghai, China

## Key words

delayed postoperative hemorrhage, operative modality, polyp size, polypectomy.

Accepted for publication 9 October 2018.

## Correspondence

Zhanju Liu, Department of Gastroenterology and Hepatology, Shanghai Tenth People's Hospital of Tongji University, Shanghai 200072, China. Email: zhanjuli66@126.com

**Declaration of conflict of interest:** None.

**Funding support:** National Natural Science Foundation of China 81300289

## Abstract

**Background and Aim:** Delayed postpolypectomy hemorrhage is relatively common, with occasional extensive blood loss, endangering life. This study aimed to determine the factors associated with postoperative hemorrhage.

**Methods:** The study was a retrospective cohort study of patients hospitalized for colonoscopic polypectomy at the Department of Gastroenterology and Hepatology, Tenth People's Hospital of Tongji University, China, between January and December 2015. Data on gender, age, bowel preparation, location, size, number of polyps, operative modality, pathology, and operation practitioner were collected. Patients were divided into two groups based on the presence or absence of postoperative hemorrhage.

**Results:** A total of 1962 polyps were detected in patients and they underwent polypectomy; hemorrhage occurred in 41 cases. A correlation was demonstrated between postpolypectomy hemorrhage and each of the following factors: polyp size and operative modality. The odds ratio (OR) was 4.535 (95% confidence interval [CI], 2.331–8.823) for 1–2-cm polyps, 4.008 (95% CI, 0.904–17.776) for 2–3-cm polyps, and 22.407 (95% CI, 5.783–86.812) for ≥3-cm polyps. Compared with argon plasma coagulation, OR was 9.128 (95% CI, 3.548–23.486) for endoscopic mucosal resection and 31.257 (95% CI, 7.009–139.395) for endoscopic submucosal dissection.

**Conclusions:** The independent risk factors for delayed postpolypectomy hemorrhage include polyp size and operative modality.

## Introduction

The incidence of colorectal polyps is high in colonoscopy screening, accounting for 25% of lesions, mostly benign.<sup>1</sup> Colorectal cancer is the third most common tumor worldwide and the fourth cause of morbidity from tumors.<sup>2</sup> The early detection and removal of polyps lead to a marked reduction in the incidence of colorectal cancer.<sup>3,4</sup> Complications following polypectomy have significantly reduced with the advancement of the submucosal injection technique,<sup>5–7</sup> but the potential for iatrogenic injury during polypectomy still exists.<sup>5</sup> The primary complications are hemorrhage and perforation,<sup>8</sup> and hemorrhage includes immediate and delayed postoperative bleeding. The incidence rate of the delayed type is 0.4–1.1%,<sup>9,10</sup> with evidently more blood loss compared with the immediate type and delayed management, endangering life. Hence, the prudence of clinicians should never be undermined.<sup>11</sup> Therefore, the identification of risk factors for delayed postpolypectomy hemorrhage is essential for the reduction of risks of complications and bleeding. A spectrum of studies exists regarding postoperative hemorrhage, but with contradictory results. The relatively unequivocal awareness is the close correlation of

polyp size with hemorrhage. More controversy of perceptions lies in the correlation with other factors, including polyp location, pathology, operative modality, concurrent diseases, and preoperative anticoagulation medications. Bowel preparation and surgeon experience are less referred.

The causal factors for bleeding include concurrent lesions, bowel preparation, location and size of polyps, operative modality, and operation clinicians. This study analyzed the risk factors from the aforementioned multiple perspectives for delayed postpolypectomy hemorrhage.

## Methods

This study was a retrospective cohort study analyzing patients who underwent colonoscopic polypectomy at the Department of Gastroenterology and Hepatology, Shanghai Tenth People's Hospital of Tongji University, China, between January and December 2015. Delayed hemorrhage was defined as more than one occurrence of overt bleeding per anus, including melena or hematochezia, 6 h after operation. Each delayed hemorrhage had undergone a therapeutic colonoscopy. The inclusion criteria were patients who underwent colonoscopic polypectomy at the

**Table 1** General information and complications of patients with delayed postpolypectomy hemorrhage.

	Uneventful ( <i>n</i> = 668)	Hemorrhage ( <i>n</i> = 41)	<i>P</i>
Age (mean ± SD)	61.00 ± 9.376	62.71 ± 11.237	0.263
Gender (%)			0.044
Male	435/668 (65.1)	33/41 (80.0)	–
Female	233/668 (34.9)	8/41 (20.0)	–
Complications			
High blood pressure	285 (42.7)	25 (61.0)	0.022
Diabetes	100 (15.0)	4 (9.8)	0.360
Coronary heart disease	50 (7.5)	5 (12.2)	0.274
Cerebrovascular accident	34 (5.1)	2 (5)	0.952

age of 18–80 years, excluding patients with familial adenomatous polyps, polyps combined with inflammatory bowel disease, or a history of colorectal surgery. At least 1-week cessation of anticoagulation medicines, such as aspirin, Plavix, and

warfarin, was instructed for all patients, and not even one patient took the specific medicine at the interval of 1 week before operation. Bowel preparation was recorded by two doctors with more than 5 years of specific practice according to Ottawa Bowel Preparation Scale.<sup>12</sup> Patient's information, including age, gender, concurrent diseases, bowel preparation, location, size and number of polyps, operative modality, pathology, and operation practitioner, was collected. Polyp size was assessed by an endoscopist and classified into four grades: <1 cm, 1–2 cm, 2–3 cm, and ≥3 cm. Polyp location was classified as rectum, left semicolon distal to the splenic flexure, and right semicolon proximal to the splenic flexure. Operative modalities comprised biopsy forceps polypectomy, argon plasma coagulation (APC), endoscopic mucosal resection (EMR), and endoscopic submucosal dissection (ESD). Pathologically, polyps were divided into three types: hyperplastic and inflammatory polyps, adenomatous polyps (tubular adenoma, villous adenoma, and villous tubular adenoma), and serrated adenoma. Surgeons were classified into three grades

**Table 2** Analysis of risk factors for delayed postpolypectomy hemorrhage.

	Uneventful ( <i>n</i> = 1921)	Hemorrhage ( <i>n</i> = 41)	<i>P</i> (two tailed)
Polyp location (%)			0.855
Colon	345/1921 (18.0)	7/41 (17.1)	
Left semicolon	998/1921 (52.0)	20/41 (48.8)	
Right semicolon	578/1921 (30.0)	14/41 (34.1)	
Polyp size (%)			<0.001
<1 cm	1561/1921 (81.3)	19/41 (46.3)	
1 cm ≤ polyp < 2 cm	308/1921 (16.0)	17/41 (41.5)	
2 cm ≤ polyp < 3 cm	41/1921 (2.1)	2/41 (4.9)	
≥3 cm	11/1921 (0.6)	3/41 (7.3)	
Operative modality (%)			<0.001
APC	1094/1921 (56.9)	5/41 (12.2)	
EMR	791/1921 (41.2)	33/41 (80.5)	
ESD	20/1921 (1.1)	3/41 (7.3)	
Forceps polypectomy	16/1921 (0.8)	0/41 (0)	
Pathology (%)			<0.001
Hyperplastic + inflammatory polyp	202/1921 (10.5)	6/41 (14.6)	
Tubular adenoma	302/1921 (15.8)	16/41 (39.0)	
Villous adenoma	18/1921 (0.9)	3/41 (7.3)	
Villous tubular adenoma	106/1921 (5.5)	7/41 (17.1)	
Malignant tumor	31/1921 (1.6)	1/41 (2.4)	
Serrated adenoma	24/1921 (1.2)	1/41 (2.4)	
Juvenile polyp	0 (0)	1/41 (2.4)	
Leiomyoma	0 (0)	1/41 (2.4)	
Carcinoid	1/1921 (0.05)	0 (0)	
Fibro-epithelial hyperplasia	2/1921 (0.1)	0 (0)	
No pathology	1233/1921 (64.2)	1/41 (2.2)	
Bowel preparation (%)			0.323
Excellent	462/1921 (24.0)	11/41 (26.8)	
Good	637/1921 (33.2)	5/41 (22.0)	
Fair	724/1921 (37.7)	17/41 (41.5)	
Poor	98/1921 (5.1)	4/41 (9.7)	
Specific operation experience (%)			0.505
5–10 years	22/1921 (1.1)	0	
10–15 years	787/1921 (41.0)	14/41 (34.1)	
>15 years	1112/1921 (57.9)	27/41 (65.9)	

APC, argon plasma coagulation; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection.

based on practice experience: 5–10 years, 10–15 years, and more than 15 years. This retrospective study had been approved by the ethnic committee of Shanghai Tenth People's Hospital of Tongji University. All data were anonymized and deidentified.

**Statistical analysis.** All data were analyzed using SPSS version 21 (SPSS, Chicago, IL, USA). Enumeration data were expressed in percentage. Regarding measurement data, normal distribution was expressed in mean  $\pm$  standard deviation, whereas nonnormal distribution was expressed in median (range). Continuous variables were statistically analyzed using the Student *t* test, and categorical variables were compared using the  $\chi^2$  test. The correlation was initially screened among all variables, followed by the binary logistic regression analysis of definitely correlated variables, and the odds ratio (OR) and 95% confidence interval (CI) were calculated for others after defining the first one as a reference value of 1. A double-tailed *P* value  $<0.05$  was considered statistically significant.

## Results

**Incidence rate of postpolypectomy hemorrhage.** A total of 1962 polyps were detected in 709 patients; hemorrhage occurred in 41 cases, with an incidence rate of 5.8%. The bleeding interval was  $1.85 \pm 1.05$  days after operation. Concurrent disease—diabetes, coronary heart disease, or cerebrovascular accident—was not correlated with delayed postpolypectomy hemorrhage, whereas hypertension patients were more susceptible to postoperative hemorrhage, as shown in Table 1.

**Risk factors for delayed postpolypectomy hemorrhage.** The risk factors for delayed postpolypectomy hemorrhage included polyp size and operative modality. No obvious correlation of delayed postpolypectomy hemorrhage was found with the pathological type, polyp location, bowel preparation, or operative experience. OR was 4.535 (95% CI, 2.331–8.823;  $P < 0.001$ ) for 1–2-cm polyps, 4.008 (95% CI, 0.904–17.776;  $P = 0.068$ ) for 2–3-cm polyps, and 22.407 (95% CI, 5.783–86.812;  $P < 0.001$ ) for  $\geq 3$ -cm polyps compared with  $<1$  cm polyps. In terms of operative modality, OR was 9.128 (95% CI, 3.548–23.486;  $P < 0.001$ ) for EMR and 31.257 (95% CI, 7.009–139.395;  $P < 0.001$ ) for ESD and 0.000 ( $P = 0.999$ ) for forceps polypectomy compared with APC. Detailed information is listed in Tables 2 and 3.

## Discussion

This study analyzed correlation factors for postpolypectomy hemorrhage. Delayed postpolypectomy hemorrhage occurred within the interval of 6 h to 4 days, at a mean time of  $1.85 \pm 1.05$  days, which was similar to the findings of Kim Hee.<sup>13,14</sup> Therefore, more caution was needed against delayed hemorrhage 1–3 days after operation. Other studies reported the incidence of delayed hemorrhage within postoperative 6 h to 17 days.<sup>15</sup> Therefore, postoperative surveillance for hemorrhage should be prolonged to avoid serious outcomes.

Referring to prior literature, the present study also displayed polyp size as a conspicuous risk factor. Min and

**Table 3** Regression analysis of risk factors for delayed postpolypectomy hemorrhage.

	Odds ratio	95% confidence interval	<i>P</i>
Pathology			
Hyperplastic/inflammatory polyp	1	–	–
Adenomatous polyp	1.879	0.756–4.669	0.174
Serrated adenoma	1.403	0.162–12.150	0.759
malignant neoplasm	1.086	0.126–9.328	0.940
Polyp size			
$<1$ cm	1	–	–
1–2 cm	4.535	2.331–8.823	$<0.001$
2–3 cm	4.008	0.904–17.776	0.068
$>3$ cm	22.407	5.783–86.812	$<0.001$
Operative modality			
APC	1	–	–
EMR	9.128	3.548–23.486	$<0.001$
ESD	31.257	7.009–139.395	$<0.001$
Forceps polypectomy	0	ND	0.999

APC, argon plasma coagulation; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection.

colleagues discovered that the incidence rate was 2.6-fold higher for polyps larger than 1 cm than for smaller polyps.<sup>16</sup> Another study reported that every 1-mm increase in polyp size increased the incidence rate by 11.6%.<sup>17</sup> Previous studies did not analyze the polyp size of various ranges but assessed the mean size. In contrast, the present study achieved a more meaningful conclusion by the classification of polyp size. Nonetheless, the limited number of  $>3$ -cm polyps could give rise to bias.

In terms of operative modality, Zhang *et al.* found that EMR or endoscopic piecemeal mucosal resection was more susceptible to hemorrhage compared with APC or biopsy forceps polypectomy, but without statistical significance.<sup>15</sup> The present study demonstrated a 9.128-fold incidence rate of hemorrhage in EMR and 31.257-fold susceptibility to hemorrhage in ESD with statistical significance. The difference could be caused by the exclusion of ESD from the comparisons in Zhang's study.

Regarding pathology, Watabe *et al.* believed that no difference in postoperative hemorrhage existed between adenoma and adenocarcinoma, with the conclusion derived from 37 cases.<sup>18</sup> In contrast, Zhang and colleagues found a close correlation between pathology and postoperative hemorrhage (4.3- and 3.3-fold), respectively, in juvenile polyposis and Peutz-Jeghers syndrome compared with inflammatory/hyperplastic polyps.<sup>15</sup> In the present study, no significant increase is found in hemorrhage in adenomatous polyps.

Some studies suggested a correlation between polyp location and postpolypectomy hemorrhage. The right semicolon was more susceptible to postoperative hemorrhage compared with the left semicolon.<sup>19,20</sup> The present study detected no conspicuous correlation between them, which could be related to higher incidences of polyps in the left semicolon of Chinese populations but nearly equal incidence in the left and right semicolon of Western populations.<sup>21</sup> In the present study, 17.9% of polyps were located in the rectum, 51.9% in the left semicolon, and 30.2% in the right semicolon.

This study had certain limitations. First, it was a single-center retrospective analysis, and data of only 1 year is not comprehensive. Second, the number of polyps  $\geq 3$  cm in size was inadequate, and hence, the results could interfere with the precision of the conclusion. Meanwhile, the assessment of bowel preparation was literally subjective, leading to potential bias on evaluation and hence a statistical error.

In summary, this study demonstrated the risk factors for postpolypectomy hemorrhage, including polyp size and operative modality. For polyps  $>1$  cm in size, the operative modality of ESD resulted in a higher incidence of hemorrhage. More clinical prudence should be taken in this regard.

## Acknowledgments

The study was funded by the National Natural Science Foundation of China (81300289). Our appreciation is specially given to all the endoscopists and colleagues involved in the study at the Department of Gastroenterology and Hepatology, Tongji University-affiliated Shanghai Tenth People's Hospital, China.

## References

- Giacosa A, Frascio F, Munizzi F. Epidemiology of colorectal polyps. *Tech. Coloproctol.* 2004; **8**(Suppl. 2): s243–7.
- Ferlay J, Soerjomataram I, Dikshit R *et al.* Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int. J. Cancer.* 2015; **136**: E359–86.
- Zauber AG, Winawer SJ, O'Brien MJ *et al.* Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. *N. Engl. J. Med.* 2012; **366**: 687–96.
- Manser CN, Bachmann LM, Brunner J, Hunold F, Bauerfeind P, Marbet UA. Colonoscopy screening markedly reduces the occurrence of colon carcinomas and carcinoma-related death: a closed cohort study. *Gastrointest. Endosc.* 2012; **76**: 110–17.
- Ian D, Wang LN, Susan A *et al.* Efficacy of colonic submucosal saline solution injection for the reduction of iatrogenic thermal injury. *Gastrointest. Endosc.* 2002; **56**: 95–9.
- Rosenberg N, Brunswick N. Submucosal saline wheal as safety factor in fulguration or rectal and sigmoidal polypi. *A.M.A. Arch. Surg.* 1955; **70**: 120–2.
- Waye JD. New methods of polypectomy. *Gastrointest. Endosc. Clin. N. Am.* 1997; **7**: 413–22.
- Parra-Blanco A, Kaminaga N, Kojima T *et al.* Hemoclipping for post-polypectomy and postbiopsy colonic bleeding. *Gastrointest. Endosc.* 2000; **51**: 37–41.
- Choung BS, Kim SH, Ahn DS *et al.* Incidence and risk factors of delayed postpolypectomy bleeding: a retrospective cohort study. *J. Clin. Gastroenterol.* 2014; **48**: 784–9.
- Wu XR, Church JM, Jarrar A, Liang J, Kalady MF. Risk factors for delayed postpolypectomy bleeding: how to minimize your patients' risk. *Int. J. Colorectal Dis.* 2013; **28**: 1127–34.
- Waye JD, Lewis BS, Yessayan S. Colonoscopy: a prospective report of complications. *J. Clin. Gastroenterol.* 1992; **15**: 347–51.
- Park JS, Kim MS, Kim H *et al.* A randomized controlled trial of an educational video to improve quality of bowel preparation for colonoscopy. *BMC Gastroenterol.* 2016; **16**: 64.
- Kim DH, Lim SW. Analysis of delayed postpolypectomy bleeding in a colorectal clinic. *J. Korean Soc. Coloproctol.* 2011; **27**: 13–16.
- Moon HS, Park SW, Kim DH, Kang SH, Sung JK, Jeong HY. Only the size of resected polyps is an independent risk factor for delayed postpolypectomy hemorrhage: a 10-year single-center case-control study. *Ann. Coloproctol.* 2014; **30**: 182–5.
- Zhang Q, An S, Chen Z *et al.* Assessment of risk factors for delayed colonic post-polypectomy hemorrhage: a study of 15553 polypectomies from 2005 to 2013. *PLoS One.* 2014; **9**: e108290.
- Kwon MJ, Kim YS, Bae SI *et al.* Risk factors for delayed post-polypectomy bleeding. *Intest. Res.* 2015; **13**: 160–5.
- Bae GH, Jung JT, Kwon JG *et al.* Risk factors of delayed bleeding after colonoscopic polypectomy: case-control study. *Korean J. Gastroenterol.* 2012; **59**: 423–7.
- Watabe H, Yamaji Y, Okamoto M *et al.* Risk assessment for delayed hemorrhagic complication of colonic polypectomy: polyp-related factors and patient-related factors. *Gastrointest. Endosc.* 2006; **64**: 73–8.
- Buddingh KT, Herngreen T, Haringsma J *et al.* Location in the right hemi-colon is an independent risk factor for delayed post-polypectomy hemorrhage: a multi-center case-control study. *Am. J. Gastroenterol.* 2011; **106**: 1119–24.
- Kim JH, Lee HJ, Ahn JW *et al.* Risk factors for delayed post-polypectomy hemorrhage: a case-control study. *J. Gastroenterol. Hepatol.* 2013; **28**: 645–9.
- Sung JJ, Lau JY, Young GP *et al.* Asia Pacific consensus recommendations for colorectal cancer screening. *Gut.* 2008; **57**: 1166–76.