

A Clinical Tool to Predict Delay Post-Polypectomy Bleeding After Resection of Colorectal Polyps

Jiaming Jiang, Shuangyan Zhu, Jin Jia, Junfeng Hu**

ABSTRACT

Background: Delay post-polypectomy bleeding (DPB) is the most frequent complication after colonoscopic polypectomy. However, only few studies have investigated the prediction of bleeding. We aimed to derive a nomogram to predict the risk of DPB.

Methods: Data on patient, polyp and polypectomy procedure were analysed. The cohort was randomly divided to the training and test group. Independent factors of DPB in the training cohort were identified by multiple logistic regression analysis and used to develop a risk score. The risk score was validated in the independent test cohort.

Results: A total of 1738 patients with 3650 polyps were included in the study. The rate of DPB in this study was 1.9% (71/3650). In the training group, the independent predictors were age (HR 0.384), prophylactic clipping (HR 0.384), polyp morphology (HR 2.546), polyp size (HR 2.491), thrombin time (HR 4.263). The derived risk score comprised age < 60 years, prophylactic clipping, polyp morphology of Ip/Isp, polyp size ≥ 10mm, TT ≥ 21 sec. In the validation cohort, the C-index for DPB prediction was 0.802. Subgroup analysis showed that prophylactic clipping is not suitable for small (<10mm) polyps.

Conclusions: We derive a readily applicable risk score that identifies patients with high risk of DPB. This score may help improving the management of those undergoing polypectomy and assist in allocating resources more cost-effectively to prevent and manage DPB. In addition, we found prophylactic clipping may increase the risk of DPB. Further well-designed researches are needed to demonstrate it.

INTRODUCTION

Colorectal cancer is a major cause of cancer morbidity and death in developed countries Stanaway JD et al. (2016). A colonoscopic polypectomy can significantly reduce the incidence of colorectal cancer Atkin WS et al. (2010). Polypectomy bleeding is a rare but important complication after polypectomy. It includes immediate and delayed bleeding. Immediate intraprocedural bleeding can generally be managed during the initial procedure, without significant patient morbidity. It is increasingly being seen as part of the procedure and should not be regarded as a complication unless it alters the clinical pathway.

Delayed polypectomy bleeding (DPB) is defined to be any bleeding occurring after the polypectomy that necessitates hospital presentation and medical management. The incidence of delayed bleeding was reported 0.6-9.4% Liaquat H et al. (2013), Burgess NG et al. (2014), Watabe H et al (2006), Zhang Q et al. (2014). DPB can be associated with significant morbidity and substantial resource utilization Burgess NG et al. (2014). It is difficult to detect initially and becomes more difficult to perform therapeutic endoscopic treatment once bleeding has occurred.

¹Department of Nuclear Medicine, State Key Laboratory of Oncology in South China, Guangdong provincial Clinical Research Center for Cancer, Sun Yat-sen University Cancer Center, 651 Dongfeng East Road, Guangzhou 510060, PR. China.

²Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Guangzhou, Guangdong, PR. China.

³Department of Nuclear Medicine, State Key Laboratory of Oncology in South China, Guangdong provincial Clinical Research Center for Cancer, Sun Yat-sen University Cancer Center, Guangzhou, China.

⁴Department of Nuclear Medicine, State Key Laboratory of Oncology in South China, Guangdong provincial Clinical Research Center for Cancer, Sun Yat-sen University Cancer Center, 651 Dongfeng East Road, Guangzhou 510060, PR. China.

Correspondence to: Dr. Junfeng Hu, Department of Nuclear Medicine, State Key Laboratory of Oncology in South China, Guangdong provincial Clinical Research Center for Cancer, Sun Yat-sen University Cancer Center, 651 Dongfeng East Road, Guangzhou 510060, PR. China. E-mail: hujf@sysucc.org.cn.

Keywords: risk score, delay post-polypectomy bleeding, colon, prophylactic clipping.

In addition, there is a lack of high-level evidence for effective interventions that prevent DPB. Some argued that a prophylactic treatment may be more cost effective and suitable for patients with high risk of DPB Bahin FF et al. (2016). From these points, it is of great value to develop a risk score to predict DPB.

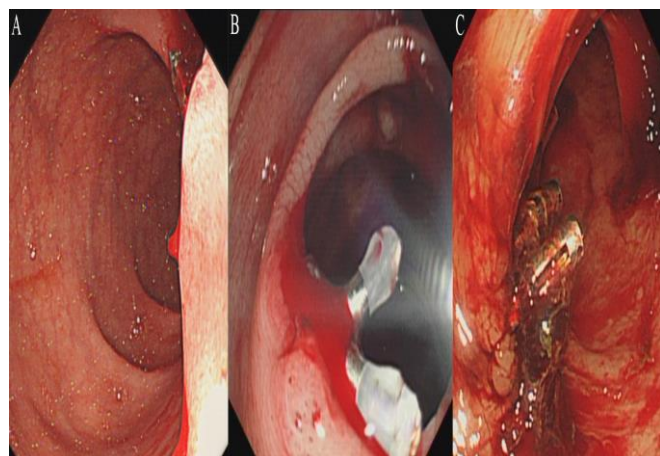
Risk scores of previous studies were limited by their applicability Bahin FF et al. (2016), Fukunaga S et al. (2019), because they aim to study particular patients. The purpose of this article is to establish a risk score with better applicability to identify high-risk populations of DPB.

METHODS

Study population

The study was approved by the institutional review board of our institution. patients treated with colonic polypectomy from October 2014 to December 2019 were enrolled. Data collection included patient-related, polyp-related and procedure-related characteristics. The gross morphology of the polyps were classified using the criteria of the Japanese Research Society Classification (1983): sessile (Is) lesions were defined as raised lesions without a stalk or pedicle; laterally spreading tumours (LSTs) were defined as large flat polyps with diameters of >10 mm; sub pedunculated (Isp) lesions were defined as those with a clearly defined neck, but with no distinct pedicle; and pedunculated (Ip) lesions were defined as those with a stalk. The polyp's locations were labelled as right colon (cecal, ascending colon, hepatic flexure, transverse colon) or left colon (splenic flexure, descending colon, sigmoid, and rectum). DPB was defined as any bleeding occurring after completion of the polypectomy necessitating hospitalization or re-intervention (repeat endoscopy, angiography, or surgery). As was shown in Figure 1, the DPB sites were identified as those that accompany with one or more of the following signs: fresh dense adherent clot, spurting, focal micro pulsatile streaming, or oozing.

Figure 1: Hemorrhage signs after polypectomy. A: focal micro pulsatile streaming from the defect; B: oozing after polypectomy. C: fresh dense adherent clot.



Patients with the following conditions will be excluded: 1. those with serious comorbid conditions, which were unsuitable to receive endoscopic therapy; 2. those with high thrombotic risk and could not cease antithrombotic therapy during peripolypectomy care; 3. those with a history of mental illness or cognitive dysfunction; 4. those with postoperative pathology suggesting malignancy that requires additional surgery.

In accordance with the guidelines from the American Society for Gastrointestinal Endoscopy Acosta RD et al. (2016), it was generally to advise all the patients to discontinue the use of aspirin or anticoagulants 5 days prior to polypectomy and recommence them 5 days after. The patients were usually discharged 3-4 days after polypectomy.

Polypectomy:

All the colonoscopy was performed using high-definition variable-stiffness colonoscopes (260/290 PCF/CF; Olympus, Tokyo, Japan) by experienced colonoscopists. Our centre used the VIO 200 D electrosurgical unit of ERBE from Germany since 2013. Endo cut Q effect 3(Cut Interval 1, Cut Duration 5) was used for resection and Forced Coag effect 2 was used for coagulation.

Different polypectomy methods were applied based on the size and morphology of polyps. Argon plasma coagulation (APC) and biopsy forceps were used to remove smaller polyps (≤ 5 mm), while snare polypectomy and endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD) were used for larger polyps. Hot or cold snare polypectomys were used to resect pedunculated or sub pedunculated polyps, sessile or flat polyps were generally removed by EMR, and the flat polyps too wide to completely remove at once were rejected by endoscopic piecemeal mucosal resection (EPMR) or ESD. If bleeding occurred during polypectomy, hot biopsy forceps or end clip were applied to control the bleeding. Submucosal fluid injection is generally established before EMR or ESD. The injection solution consisted of diluted methylene blue, hyaluronic acid and mannitol. The usage of prophylactic clipping to the mucosal defect was determined by the surgeons' experience.

Statistical analysis

The statistical software (IBM SPSS Statistics, Version 22; IBM, Armonk, NY) was used to analyse the data. Frequencies and percentages with 95% confidence intervals (95% CIs) where relevant were used for categorical variables. The cohort was divided at random into training and test groups. Categorical variables were classified based on clinical findings. All the optimal cut-off points in our study were evaluated by reference ranges and continuous variables were transformed to categorical variables.

Multiple logistic regression with backward stepwise variable selection was used to identify the independent predictors of DPB in the training cohort. Candidate variables for inclusion in the model were those demonstrating independent association with DPB in the training cohort with P values <0.05.

Odds ratios (ORs) and their 95% CIs were used to quantify the association between the independent risk factors and DPB in the training cohort, and Hosmer–Lemeshow test was used to assess the goodness-of-fit of the model.

A risk score was developed by assigning a weight to each independent risk factor category based on the best fitting multiple logistic regression model for the training cohort.

The performance of the risk score and classification was then externally validated in the independent test cohort. A two tailed P value < 0.05 was considered statistically significant.

RESULTS

Clinicopathological characteristics of patients

From October 2014 to December 2019, a total of 1738 patients with 3650 polyps were included in the study. The median age of patients was 58 years (Interquartile rang, IQR 51–65 years) and 66.3% was male. The mean and median size of the polyps was 11 and 10 mm (IQR 6–15 mm), respectively. The size of 85% polyps was less than 10mm. The morphology of 2340 polyps were Ip/Isp and 75.2% of the polyps was pathologically diagnosis as adenoma. 2694 polyps were treated by hot snare polypectomy or EMR, 243 by ESD, 659 by biopsy force or APC, and 54 by cold snare polypectomy. The rate of DPB in this study was 1.9% (71/3650). Lesions were randomly assigned to the training (2800 lesions) or test cohorts (850 lesions). As shown in Table 1, characteristics of the lesions and demographic data of patients corresponding to polyps were similar between the training and the test group.

Table 1: Baseline clinical features.

	Derivation cohort		Validation cohort	
	Mean/ Number	SD/Percentage	Mean/ Number	SD/Percentage
DPB				
No	2742	97.93%	837	98.47%
Yes	58	2.07%	13	1.53%
Age, year				
<60	1214	43.36%	367	43.18%
≥60	1586	56.64%	483	56.82%
Sex				
Male	1951	69.68%	609	71.65%
Female	849	30.32%	241	28.35%
Hypertension				
No	1965	70.18%	604	71.06%
Yes	821	29.32%	245	28.82%
Diabetes mellitus				
No	2484	88.71%	769	90.47%
Yes	302	10.79%	80	9.41%
Cardiovascular disease				
No	2707	96.68%	812	95.53%
Yes	93	3.32%	38	4.47%
Anticoagulate/antiplatelet agent usage				
No	2677	95.61%	809	95.18%
Yes	123	4.39%	41	4.82%
PT, second				
<13.5	2777	99.18%	842	99.06%
≥13.5	23	0.82%	8	0.94%

APTT, second				
<34.0	2717	97.04%	821	96.59%
≥34.0	83	2.96%	29	3.41%
TT, second				
<21.0	2770	98.93%	846	99.53%
≥21.0	30	1.07%	4	0.47%
Fbg, g/L				
<1.8	56	2.00%	16	1.88%
≥1.8	2744	98.00%	834	98.12%
PLT,109/L				
<100.0	46	1.64%	8	0.94%
≥100.0	2754	98.36%	842	99.06%
Polypectomy methods				
Hot snare polypectomy/EMR	2070	73.93%	624	73.41%
ESD	187	6.68%	56	6.59%
Biopsy forcep/APC	499	17.82%	160	18.82%
Cold snare polypectomy	44	1.57%	10	1.18%
Use of microprocessor-controlled electrosurgical generator				
No	531	18.96%	187	22.00%
Yes	2269	81.04%	663	78.00%
Prophylactic clipping				
No	1715	61.25%	549	64.59%
Yes	1085	38.75%	301	35.41%
polyp morphology				
Is/LST	1743	62.25%	597	70.24%
Ip/Isp	1057	37.75%	253	29.76%
Polyp size				
<10mm	2377	84.89%	784	92.24%
≥10mm	423	15.11%	66	7.76%
histology				
Inflammatory/hyperplastic	418	14.93%	132	15.53%
Adenomatous	2144	76.57%	654	76.93%
secreted	69	2.46%	19	2.24%
Atypia	157	5.61%	43	5.06%
other	12	0.43%	2	0.24%
location				
Right	1262	45.07%	395	46.47%
Left	1538	54.93%	455	53.53%

Is: sessile, Isp: sub pedunculated, Ip: pedunculated, LSTs: laterally spreading tumors, EMR: endoscopic mucosal resection, ESD: endoscopic submucosal dissection: Argon plasma coagulation.

Univariate and multivariate analysis for the biomarker selection

In Table 2. Univariable analysis of the training cohort identified the following variables for inclusion in the multiple logistic regression analysis of DPB: age, TT, polyp morphology, polyp size, the use of prophylactic clipping and the use of microprocessor-controlled electrosurgical

generator. Multivariable analysis showed that age (P=0.001, HR: 0.384, 95% CI: 0.217-0.680), prophylactic clipping (P=0.001, HR: 0.384, 95% CI: 0.217-0.680), polyp morphology (P=0.005, HR: 2.546, 95% CI: 1.330-4.870), polyp size (P=0.001, HR: 2.491, 95% CI: 1.418-4.376), TT (P=0.026, HR: 4.263, CI: 1.189-15.285) were independent prediction factors for DPB.

Table 2: Univariate and multivariate cox hazards analysis between clinical features and DPB.

Characteristics	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age, year				
<60/≥60	0.337(0.192-0.591)	<0.001*	0.384(0.217-0.680)	0.001*
Sex				
Male/Female	0.659(0.353-1.227)	0.238		
Hypertension				
No/ Yes	1.107(0.629-1.947)	0.837		
Diabetes mellitus				
No/ Yes	0.967(0.411-2.273)	0.999		
Cardiovascular disease				
No/ Yes	0.505(0.069-3.689)	0.752		
Anticoagulate/antiplatelet agent usage				
No/ Yes	0.377(0.052-2.744)	0.497		
PT, second				
<13.5/≥13.5	2.169(0.287-16.369)	0.972		
APTT, second				
<34.0/≥34.0	1.815(0.556-5.925)	0.541		
TT, second				
<21.0/≥21.0	5.485(1.616-18.621)	0.015*	4.263(1.189-15.285)	0.026
Fbg, g/L				
<1.8/≥1.8	0.563(0.134-2.364)	0.747		
PLT,109/L				
<100.0/≥100.0	1.022(1.0161-1.027)	0.636		
Use of microprocessor-controlled electrosurgical generator				
No/ Yes	0.974(0.968-0.981)	<0.001*	0.000(0.000-0.000)	0.992
Prophylactic clipping				
No/ Yes	0.195(0.106-0.357)	<0.001*	0.338(0.175-0.652)	0.001*
polyp morphology				
Is, LST/Is, LST	4.885(2.700-8.838)	<0.001*	2.559(1.340-4.883)	0.004*
Polyp size				
<10mm/≥10mm	4.462(2.625-7.583)	<0.001*	2.555(1.452-4.495)	0.001*
location				
Right/Left	1.254(0.737-2.134)	0.481		

Development and Validation of the Prediction Model

The nomogram was constructed to predict DPB on the basis of the identified factors (Figure 2).

The risk score derived this best fitting model to weight each included factor is: age<60 years weight 66 points, prophylactic clipping weight 78 points, polyp morphology of Ip/Isp weight 64 points, polyp size≥10mm weight 63 points, TT≥21 sec weight 99 points. The validation of nomogram was consisted of discrimination and calibration by using the derivation and validation set. Discrimination was performed by using a concordance index(C-index).

Calibration was evaluated by comparing the means of risk prediction with estimating of predicted with observed DPB, with the x-axes are actual DPB estimated by the nomogram, the y-axes are observed DPB.

In the derivation set, the C-index for DPB prediction was 0.805, and the calibration curve suggested that this model was a good fit to the data. In the validation cohort, the C-index for DPB prediction was 0.802, and the calibration curve showed an optimal agreement between the prediction by nomogram and actual observation (Figure 3).

Figure 2: The prediction nomogram for delay post-polypectomy bleeding, including age, prophylactic clipping, polyp morphology, polyp size, TT. Each patient's probability of delay post-polypectomy bleeding is located on each variable axis, and a line is drawn upward to determine the number of points received for each variable value.

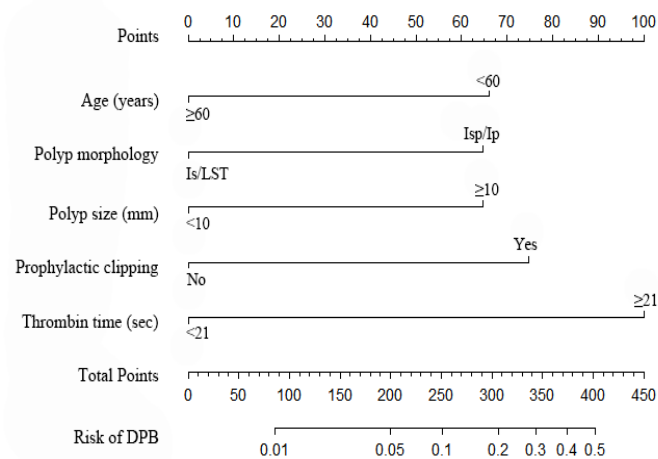


Figure 3: The calibration curve for delay post-polypectomy bleeding. Nomogram-predicted probability of post-polypectomy bleeding is showed on the x-axis; actual post-polypectomy bleeding is plotted on the y-axis.

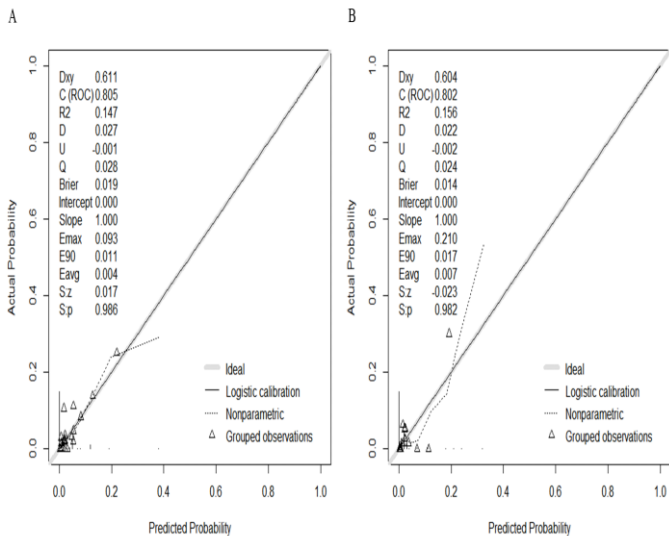


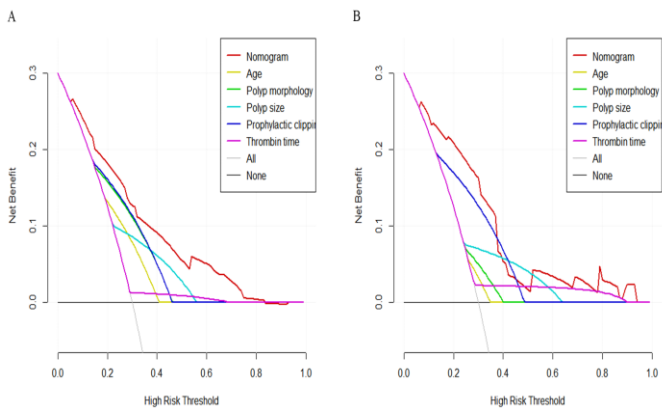
Table 3: Subgroup analysis for prophylactic clipping

Small, Is/LST (N=1575)	Non-bleeding group (Number, %)	Bleeding group (Number, %)	P <0.01*
Clipping	392 (24.89%)	9 (0.57%)	
Non-clipping	1173 (74.48%)	1 (0.06%)	
Small, Isp/Ip (N=802)			0.14
clipping	404 (50.37%)	16 (2.00%)	
Non-clipping	375 (46.76%)	7 (0.87%)	
Large, Is/LST (N=168)			0.66

Decision curve analysis

The decision curve analysis for the nomogram and constructed features are showed in Figure 4.

Figure 4: Decision curve analysis of clinical use assessment of the nomogram in the primary group. The Y-axis represented the net benefit. The method was the best for feature selection if it had the highest net benefit. The nomogram achieved the highest net benefit compared with the age, prophylactic clipping, polyp morphology, polyp size and TT.



The decision curve presented that if the threshold probability of a patient is > 10%, the developed nomogram and features in predicting DPB is more benefit than all patients dead scheme or none patients' dead scheme. Furthermore, the net benefit was comparable, the nomogram in predicting DPB is more benefit than that of constructed features in this range.

Subgroup analysis for prophylactic clipping

Regarding to the effect of prophylactic clipping, we process subgroup analysis basis on the size and the morphology of the polyps. As was shown in Table 3, the use of prophylactic clipping significantly increases the rate of DPB in the polypectomy of small non-pedunculated polyps ($p<0.01$). In the analysis of small polyps with a stalk, there was a trend to increase the rate of DPB in the clipping group, even though it is not significant ($p=0.14$). Moreover, there was not significant different in the rate of DPB between the clipping and the non-clipping group for larger polyps ($\text{size}\geq 10\text{mm}$).

Clipping	52 (30.95%)	2 (1.19%)	
Non-clipping	111(66.07%)	3 (1.79%)	
Large, Isp/Ip (N=255)			0.99
clipping	193 (75.69%)	17 (6.67%)	
Non-clipping	42 (16.47%)	3 (1.18%)	

“small” means polyp size<10mm;” large” means polyp size ≥10mm.

Is sessile, Isp sub pedunculated, Ip pedunculated, LSTs laterally spreading tumours

DISCUSSION

DPB is the most common complication of colonoscopic polypectomy. In this study, we assessed the incidence, predictors of DPB and developed a risk score to distinguish high-risk patients. A total of 4% of the patients and 2% of all polyps retrieved developed DPB. This consists with previous studies Liaquat H et al. (2013), Burgess NG et al. (2014), Watabe H et al (2006), Zhang Q et al. (2014). Young age (<60 years), polyp size > 10 mm, polyp morphology (Ip or Isp) and Thrombin time (TT) were independent risk factors for DPB. Furthermore, we analysis the effect of prophylactic endoscopic clipping in the Prevention of DPB.

As for patient-related factors, we found that young age (<60 years) was associated with DPB in the multivariate analysis. Previous studies have had varying results on the relationship between age and DPB, with some reporting an influence Park SK et al. (2018), Sorbi D et al. (2000), but the majority did not find it to affect bleeding rates Watabe H et al. (2006), Sawhney MS et al. (2008), Rutter MD et al. (2014), Jaruvongvanich V et al. (2017), Zhang et al. reported that younger age have higher rate of DPB in their univariate analysis. However, they did not include age in their multivariate analysis Watabe H et al. (2006), Sawhney MS et al. (2008), Rutter MD et al. (2014), Jaruvongvanich V et al. (2017). Park et al. reported that young age is a risk factor for DPB after adjustment for other patient-, procedure-, and polyp-related factors Park SK et al. (2018). Our result is similar to these studies, but the reason for the influence of young age on delayed bleeding in our study is unclear. We presumed that it might be associated with medical compliance of patients. This suggests that postoperative education should be strengthened. Previous studies have paid less attention to the differences in blood test of patients. In this study, we found that prolonged thrombin time (TT) is an independent risk factor for DPB. TT refers to the time for blood to coagulate after addition of standardized thrombin to the plasma. Accordingly, it is easy to understand that prolonged TT relates to high risk of bleeding. In the present study, we found that the use of antiplatelet or anticoagulants is not a risk factor of DPB.

This consists with the previous study Sawhney MS et al. (2008), Moon HS et al. (2014), Manocha D et al. (2012). Of note, patients included in this study were all asked to cease antiplatelet or anticoagulants 5 days before polypectomy and recommence them 5 days after.

Moreover, the result may be underpowered because of the low percentage of patients with the medical history of antithrombotic therapy. The conclusion needs more high-quality evidences to demonstrate.

As for polyp-related factor, polyp size>10mm and pedunculated polyp were found to be associated with DPB. Polyp size was generally recognized to be the most reliable predictor of DPB in several previous studies Watabe H et al. (2006), Jaruvongvanich V et al. (2017), Moon HS et al. (2014), Consolo P et al. (2008). we found that polyp size larger than 10 mm is an independent risk factor of DPB. Similarly, a meta-analysis found a 3.4-fold increased risk of bleeding in patients with resected polyp size ≥ 10 mm. In addition, several investigators have indicated that polyp morphologic features appear to be important in contributing to DPB Park SK et al. (2018), Sawhney MS et al. (2008). In this study, we found Ip/Isp lesions have higher risk of DPB than the non-pedunculated lesions. Our result consists with study from Park and his workmates Park SK et al. (2018), in which the Ip/Isp polyps were reported to be correlate with major bleeding.

As for procedure-related factors, polypectomy methods are important procedure-related factors of DPB. In general, the selection of polypectomy methods depends on the size and the morphology of polyps. Although in univariate analysis polypectomy methods was showed to be significantly different in the rate of DPB, the final multivariate analysis shows that polypectomy method is not a risk factors. This consists with previous study Zhang Q et al. (2014), Choung BS et al. (2013).

The effect of prophylactic clipping to prevent DPB is still under debated. We found that prophylactic clipping significantly increases the risk of DPB, especially for polypectomies of sessile polyp<10mm. Fares et al. reported that prophylactic clipping may reduce DPB following EMR of large colorectal lesions (>20mm) Ayoub F et al. (2019). However, several meta-analyses reported that the rate of DPB is similar between cases with clipping vs no clipping Nishizawa T et al. (2017), Park CH et al. (2016), Forbes N et al. (2019). A prospective randomized study reported that the prophylactic clipping in polypectomies of large pedunculated polyps does not reduce the risk of post-polypectomy bleeding and leads to an unacceptable risk of mucosal burns and perforation Quintanilla E et al. (2012).

The subgroup analysis in our research showed that prophylactic clipping significantly increases the risk of DPB in polypectomies of sessile polyp<10mm ($p<0.01$). The reason is yet unclear. We presumed that it may be associated with slippage of the clip from the defect or mucous damage caused by friction between clip and the intestine. The protective effect of prophylactic clipping needs more well-designed RCTs to demonstrated.

For bleeding is the most common postpolypectomy-related adverse event, various prophylactic endoscopic therapies are conventionally used to prevent it. However, there is limited high-level evidence to support prophylactic interventions in the prevention of DPB.

A network meta-analysis showed that any prophylactic therapies, such as mechanical therapy or injection therapy, did not offer a significant benefit for reducing DPB Park CH et al. (2016). From a health economics standpoint, a prophylactic treatment may not be cost effective and suitable for all patients receiving polypectomy.

It is necessary to develop a risk score to distinguish high-risk patients Corte CJ et al. (2014). Previous studies Bahin FF et al. (2016), Fukunaga S et al. (2019), had developed risk scores for particular patients with large lesions (polyp size>20mm) or with the use of antithrombotic agent. However, the applicability of these scores is limited. It is necessary to develop a more applicable score system to predict the risk of DPB. A valid score system may be valuable in the design of studies evaluating interventions to prevent DPB. Moreover, it would be of economic benefit because allocation of resources to prevent and manage DPB would be more helpful in patients at high risk of DPB.

Our study has some limitations. First, the polyp-related factors may be over-power because we investigated 3650 polyps in 1738 patients. Accordingly, patient-related factors, such as age, may have been duplicated.

Second, the majority cases of prophylactic clipping are polypectomies of Is/LST polyp<10mm (1575/3650, 43.2%). the damage effect of clipping may be overestimated. Third, this score was derived in a randomly selected half of our cohort and validated in the remaining half. Further external validation in prospectively designed studies is needed.

CONCLUSIONS

we derive a risk score consist of five components, such as age, TT, polyp size, polyp morphology and the usage of prophylactic clipping. This score may assist in distinguishing high risk DPB patients to whom allocating resources to prevent and manage DPB would be more cost-effective. In addition, we found prophylactic clipping may increase the risk of DPB. Further well-designed researches are needed to demonstrate it.

DECLARATIONS

Conflicts of interest

None.

Funding

No funding was received for conducting this study.

Ethics

Ethics Committee of Sun Yat-sen University Cancer Center.SL-G2024-007-01

Consent

Informed consent was obtained from all individual participants included in the study. participants informed consent regarding publishing their data. All authors approved the final manuscript and submission to this journal.

REFERENCES

1. Stanaway JD, Flaxman AD, Naghavi M, et al. 2016. The global burden of viral hepatitis from 1990 to 2013: findings from the Global Burden of Disease Study 2013. *Lancet*. 388(10049):1081-88.
2. Atkin WS, Edwards R, Kralj-Hans I, et al. 2010. Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicenter randomized controlled trial. *Lancet*. 375(9726):1624-33.
3. Liaquat H, Rohn E, Rex DK. 2013. Prophylactic clip closure reduced the risk of delayed post polypectomy hemorrhage: experience in 277 clipped large sessile or flat colorectal lesions and 247 control lesions. *Gastrointest Endosc*. 77(3):401-7.
4. Burgess NG, Metz AJ, Williams SJ, et al. 2014. Risk factors for intraprocedural and clinically significant delayed bleeding after wide-field endoscopic mucosal resection of large colonic lesions. *Clin Gastroenterol Hepatol*. 12(4):651-61. e1-3.
5. Watabe H, Yamaji Y, Okamoto M, et al. 2006. Risk assessment for delayed hemorrhagic complication of colonic polypectomy: polyp-related factors and patient-related factors. *Gastrointest Endosc*. 64(1):73-78.
6. Zhang Q, An S, Chen Z, et al. 2014. Assessment of risk factors for delayed colonic post-polypectomy hemorrhage: a study of 15553 polypectomies from 2005 to 2013. *PLoS One*. 9(10): e108290.
7. Burgess NG, Williams SJ, Hourigan LF, et al. 2014. A management algorithm based on delayed bleeding after wide-field endoscopic mucosal resection of large colonic lesions. *Clin Gastroenterol Hepatol*. 12(9):1525-33.

8. Bahin FF, Rasouli KN, Byth K, et al. 2016. Prediction of Clinically Significant Bleeding Following Wide-Field Endoscopic Resection of Large Sessile and Laterally Spreading Colorectal Lesions: A Clinical Risk Score. *Am J Gastroenterol.* 111(8):1115-22.
9. Fukunaga S, Nagami Y, Ohira M, et al. 2019. Su1690 Orbit Score Predicts Major Bleeding After Colorectal Polypectomy in Patients Receiving Oral Anticoagulation Therapy. *Gastrointest Endosc.* 89: B381.
10. 1983. General rules for clinical and pathological studies on cancer of the colon, rectum and anus. Part II. Histopathological classification. Japanese Research Society for Cancer of the Colon and Rectum. *Jpn J Surg.* 13(6):574-98.
11. Acosta RD, Abraham NS, Chandrasekhara V, et al. 2016. The management of antithrombotic agents for patients undergoing GI endoscopy. *Gastrointest Endosc.* 83(1):3-16.
12. Park SK, Seo JY, Lee MG, et al. 2018. Prospective analysis of delayed colorectal post-polypectomy bleeding. *Surg Endosc.* 32(7):3282-89.
13. Sorbi D, Norton I, Conio M, et al. 2000. Postpolypectomy lower GI bleeding: descriptive analysis. *Gastrointest Endosc.* 51(6):690-6.
14. Sawhney MS, Salfiti N, Nelson DB, et al. 2008. Risk factors for severe delayed postpolypectomy bleeding. *Endoscopy.* 40(2):115-9.
15. Rutter MD, Nickerson C, Rees CJ, et al. 2014. Risk factors for adverse events related to polypectomy in the English Bowel Cancer Screening Programme. *Endoscopy.* 46(2):90-7.
16. Jaruvongvanich V, Prasitlumkum N, Assavapongpaiboon B, et al. 2017. Risk factors for delayed colonic post-polypectomy bleeding: a systematic review and meta-analysis. *Int J Colorectal Dis.* 32(10):1399-406.
17. Moon HS, Park SW, Kim DH, et al. 2014. 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.* 30(4):182-5.
18. Manocha D, Singh M, Mehta N, et al. 2012. Bleeding risk after invasive procedures in aspirin/NSAID users: polypectomy study in veterans. *Am J Med.* 125(12):1222-7.
19. Consolo P, Luigiano C, Strangio G, et al. 2008. Efficacy, risk factors and complications of endoscopic polypectomy: ten-year experience at a single center. *World J Gastroenterol.* 14(15):2364-9.
20. Choung BS, Kim SH, Ahn DS, et al. 2013. Incidence and risk factors of delayed postpolypectomy bleeding: a retrospective cohort study. *J Clin Gastroenterol.* 48(9):784-9.
21. Ayoub F, Westerveld DR, Forde JJ, et al. 2019. Effect of prophylactic clip placement following endoscopic mucosal resection of large colorectal lesions on delayed polypectomy bleeding: A meta-analysis. *World J Gastroenterol.* 25(18):2251-63.
22. Nishizawa T, Suzuki H, Goto O, et al. 2017. Effect of prophylactic clipping in colorectal endoscopic resection: A meta-analysis of randomized controlled studies. *United European Gastroenterol J.* 5(6):859-867.
23. Park CH, Jung YS, Nam E, et al. 2016. Comparison of Efficacy of Prophylactic Endoscopic Therapies for Postpolypectomy Bleeding in the Colorectum: A Systematic Review and Network Meta-Analysis. *Am J Gastroenterol.* 111(9):1230-43.
24. Forbes N, Frehlich L, James MT, et al. 2019. Routine Prophylactic Endoscopic Clipping Is Not Efficacious in the Prevention of Delayed Post-Polypectomy Bleeding: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *J Can Assoc Gastroenterol.* 2(3):105-17.
25. Quintanilla E, Castro JL, Rabago LR, et al. 2012. Is the use of prophylactic hemoclips in the endoscopic resection of large pedunculated polyps useful? A prospective and randomized study. *J Interv Gastroenterol.* 2(4):183-188.
26. Corte CJ, Burger DC, Horgan G, et al. 2014. Postpolypectomy haemorrhage following removal of large polyps using mechanical haemostasis or epinephrine: a meta-analysis. *United European Gastroenterol J.* 2(2):123-30.