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Hemostatic prophylaxis and colonoscopy outcomes for patients with bleeding disorders: A retrospective cohort study and review of the literature

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Abstract

Introduction: Hemostatic prophylaxis (HP) is recommended for patients with bleeding disorders (PWBD) before invasive procedures. However, evidence-based guidelines are needed to determine optimal HP strategies.

Aim: To determine outcomes of HP for PWBD undergoing colonoscopy.

Methods: We undertook a retrospective cohort study of HP and outcomes of colonoscopy procedures performed between 9 November 1993 and 13 February 2018 for PWBD who received care in the Mayo Clinic Comprehensive Hemophilia Treatment Center.

Results: During the study period, 73 PWBD (58 with milder phenotypes: haemophilia, von Willebrand disease [subtypes 1 and 2; II, VII and XI deficiency]) underwent 141 procedures. Preprocedural HP was given to 61%, and interventions were performed in 47%. Of the 39% without preprocedural HP, postprocedural HP was given for 11%. One major (0.7%; 6 days postprocedure despite HP) and 10 minor (7%) bleeding complications occurred, which tended to be in patients with severe disease and/or after excision of larger polyps. There was no significant difference in the rate of bleeding complications with or without preprocedural HP (8.1% vs 5.5%, respectively; $P = .74$, Fisher's exact test).

Conclusion: The low bleeding rates in our cohort suggest that preprocedure HP may be withheld for patients with mild bleeding disorders who undergo colonoscopy with a low likelihood of requiring an intervention or who require only low-risk intervention. This strategy may be best used in experienced centres, provided optimal local hemostasis measures are undertaken and postprocedural HP is rapidly available if high-risk intervention is required. Further studies are needed to determine optimal evidence-based HP strategies for PWBD undergoing colonoscopy.

KEYWORDS

colonoscopy, haemophilia, prophylaxis, von Willebrand disease

1 | INTRODUCTION

Increased longevity of patients with inherited bleeding disorders (PWBD) has led to an increase in typical age-related comorbidities.[1] Many PWBD undergo colonoscopy for various indications including colorectal cancer screening, evaluation of gastrointestinal bleeding, polyp surveillance or other gastrointestinal symptoms. Screening for colorectal cancer typically begins at 50 years and may initially consist of non-invasive or invasive modalities. Any abnormal non-invasive screening test result is usually followed up with a colonoscopy[2,3] because of its effectiveness as a diagnostic screening tool and therapeutic procedure.[4]

The 2018 American Thrombosis and Hemostasis Network (ATHN) research report stated that there were over 12 000 people between 30 and 74 years in the United States with bleeding disorders (The American Thrombosis and Hemostasis Network, unpublished data). Considering age-appropriate screening recommendations, these data suggest that over 12 000 colonoscopy procedures may be performed in PWBD over the next 10 years, for which periprocedural haemostatic management is critical for optimal outcomes. However, lack of prospective controlled clinical trials precludes generation of evidence-based guidelines. Periprocedural haemostatic prophylaxis (HP) is often recommended on the basis of expert opinion. Yet, not all colonoscopy procedures result in interventions, such as polypectomy or biopsy, and some interventions pose an extremely low risk of bleeding complications. Therefore, haemostatic agents may be administered unnecessarily, potentially increasing the risk of thrombosis from oversupplementation as well as out-of-pocket expenses for patients.

We reviewed our institutional experience to better understand the outcomes of periprocedural HP for PWBD undergoing colonoscopy.

2 | METHODS

2.1 | Study setting, population and design

The Mayo Clinic Institutional Review Board approved this retrospective cohort study and waived informed consent for patients who provided research authorization. We reviewed electronic health records of consenting PWBD who had outpatient colonoscopy procedures between 9 November 1993 and 13 February 2018 and who received follow-up care in the haemophilia treatment centre (HTC) at Mayo Clinic, Rochester, Minnesota. Criteria for diagnosis and classification of von Willebrand disease (VWD) and haemophilia conformed to recommendations from the appropriate Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis.[5,6] We defined high-risk bleeding disorders as severe factor deficiencies, platelet function defects, dysfibrinogenemia and acquired von Willebrand syndrome (AVWS).

2.2 | Providers, indications for colonoscopy and HP

Ordering providers were categorized as HTC providers (haematologists providing care for PWBD) or non-HTC providers (non-haematologists). If a colonoscopy was ordered by a non-HTC provider, the health record was reviewed for documentation of contact with HTC for advice on periprocedural haemostatic management. Documentation of HP was obtained from the medication administration record. Indications for colonoscopy were obtained from the procedure note and the electronic order. Periprocedural HP was defined as administration of haemostatic agents before or after the procedure, or both; use of a haemoclip was considered an additional precaution.

2.3 | Complications related to colonoscopy

The definition of major bleeding complications conformed to the recommendations of the International Society on Thrombosis and Haemostasis, Scientific and Standardization Committee, defined as bleeding that was fatal or occurring in a critical organ, resulting in a drop in haemoglobin level of 2 g/dL or requiring a second intervention to control the bleeding.[7] All other bleeding complications were considered minor. In addition, bleeding complications were categorized as occurring during the procedure (procedural), in the postprocedure recovery room (immediate postprocedural) or up to 30 days postprocedure (delayed).

2.4 | Data collected and statistical analysis

Data collected included patient demographic characteristics, bleeding disorder–specific information, ordering providers, indication for and findings on colonoscopy, interventions (if any) and periprocedural HP strategy. The latter included intravenous (IV) desmopressin acetate (DDAVP, 0.3 μg/kg body weight); intranasal DDAVP (300 μg); IV plasma-derived or recombinant coagulation factor concentrates; and orally administered antifibrinolytic agents (epsilon aminocaproic acid [EACA] and tranexamic acid [TXA]). Data were collected in an Excel database (Microsoft Corp) for summary calculations (median, range and mean). The Fisher exact test was used to further analyse categorical data for statistical differences. JMP statistical software (SAS Institute Inc) was used for the calculations. A P value of <.05 was set as the α level for statistical significance.

3 | RESULTS

3.1 | Demographic characteristics

During the study period, 73 patients (30 women) with bleeding disorders underwent 141 colonoscopy procedures. Median age (range) at the time of the procedure was 62 (3-87) years. The median number

of procedures per patient was 2 (1-6): 41 patients (56%) underwent one procedure; 32 patients (44%) had more than one procedure. The distribution of types of bleeding disorders is shown in Table 1. There was heterogeneity in the types of bleeding disorders; however, we considered mild bleeding disorders as follows: mild/moderate haemophilia and symptomatic carriers of haemophilia A (HA): 21; VWD subtypes 1 and 2:30; deficiencies of factors II, VII and XI: 1, 2 and 4, respectively (total 58). We considered the following to be severe bleeding disorders: severe HA with or without inhibitor: 4; type 3 VWD: 3; AVWS: 4; dysfibrinogenemia: 1; platelet function defects: 3 (total 15). Overall, the most common indications for colonoscopy were follow-up of polyps (n = 38, 27%), colorectal cancer screening (n = 33, 23%), evaluation of gastrointestinal bleeding (n = 30, 21%) and anaemia with or without iron deficiency (n = 15, 11%; Table 2).

TABLE 1 Distribution of bleeding disorders and coagulation factor levels

Diagnosis	Patients, no. (%) (N = 73)	Coagulation factor level, mean (range), %[a]
Haemophilia		
Mild HA	13 (18)	25 (9-45)
Moderate HA	2 (3)	4 and 5
Severe HA	3 (4)	<1
Severe HA with inhibitor	1 (1)	<1
Mild HB	5 (7)	16 (10-23)
Moderate HB	1 (1)	4
Factor XI deficiency	4 (5)	21 (6-45)
von Willebrand disease		
Type 1	22 (30)	FVIII, 72 (23-126) VWF:RCo, 36 (12-62) VWF:Ag, 39 (7-65)
Type 2A, 2B, 2M	3 (4), 4 (5), 1 (1)	FVIII, 88 (43-149) VWF:RCo, 35 (28-52) VWF:Ag, 49 (26-79)
Type 3	3 (4)	FVIII, 23 (6-56) VWF:RCo, <12 VWF:Ag, 7 (2-12)
AVWS	4 (5)	FVIII, 50 (19-126) VWF:RCo, <12 and 34 VWF:Ag, 22 (9-35)
Other factor deficiencies		
Factor VII deficiency	2 (3)	21 and 40
Factor II deficiency	1 (1)	5
Dysfibrinogenemia	1 (1)	Cl:44 mg/dL, PT:438 mg/dL
Platelet function defects		
Glanzmann thrombasthenia	1 (1)	NA
Platelet procoagulant defect	1 (1)	NA
Hermansky-Pudlak syndrome	1 (1)	NA

Abbreviations: Ag, antigen; AVWS, acquired von Willebrand syndrome; Cl, Clauss fibrinogen; FVIII, factor VIII; HA, haemophilia A; HB, haemophilia B; NA, not applicable; PT, prothrombin time derived; RCo, ristocetin cofactor; VWF, von Willebrand factor.

[a]For some diagnoses, presenting mean (range) was not possible because of too few patients in the category. In those instances, only % is given.

3.2 | Ordering providers, periprocedural HP and procedural interventions

Of the 141 procedures, 92 (65%) were ordered by non-HTC providers, with gastroenterology and general internal medicine services accounting for the majority (53%). Of these 92 procedures, the HTC was contacted for only 44 (48%). Of the total cohort, preprocedural HP was given for 86 of 141 (61%) procedures: 38 of 49 (78%) ordered by HTC providers and 48 of 92 (52%) ordered by non-HTC providers (P = .004, Fisher's exact test).

We analysed how often preprocedure HP was given for the 92 procedures ordered by non-HTC providers based on documentation of contact with the HTC. The HTC was notified of 44/92 procedures, and preprocedure HP was given in 86% (38/44). However, for 48/92 procedures, for which HTC was not notified, preprocedure HP was given for only 21% (10/48). Of the 3 patients with severe HA, only

TABLE 2 Intervention by indication for colonoscopy

Indication	Procedural intervention, no. (%)	No procedural intervention, no. (%)
Polyps, follow-up	24 (63)	14 (37)
Colorectal cancer screening	9 (27)	24 (73)
GI bleeding	8 (27)	22 (73)
Diarrhoea	8 (89)	1 (11)
Iron deficiency anaemia	2 (25)	6 (75)
Anaemia	6 (86)	1 (14)
Colon cancer, follow-up	3 (60)	2 (40)
Crohn disease	2 (50)	2 (50)
Abnormal imaging, abdominal CT scan	1 (50)	1 (50)
Ulcerative colitis, follow-up	1 (50)	1 (50)
Abnormal imaging, colon radiograph	0 (0)	1 (100)
Abdominal pain	1 (100)	0 (0)
Abnormal virtual colonoscopy	1 (100)	0 (0)

Abbreviations: CT, computed tomography; GI, gastrointestinal.

1 was prescribed a programme of prophylactic factor infusions, and the colonoscopy was scheduled on a day that the patient was due for his regular prophylaxis.

An intervention was performed in 66 of 141 (47%) procedures: 48 (73%) polypectomies, 15 (23%) biopsies and 3 (5%) argon plasma coagulation (APC) of arteriovenous malformations. The intervention frequency by indication for colonoscopy is shown in Table 2. Overall, there was no difference in rate of bleeding complications based on preprocedure HP administration status; postprocedure bleeding was observed in 7 of 86 (8.1%) procedures in which preprocedural HP was administered vs 3 of 55 (5.5%) procedures in which no preprocedural HP was administered ($P = .74$, Fisher's exact test).

3.3 | Bleeding complications

Of 11 bleeding complications, 1 was major and 10 were minor. The frequency of interventions categorized by preprocedural HP and outcomes of bleeding complications are summarized in Table 3 and Figures 1 and 2. A 49-year-old man with a history of Glanzmann thrombasthenia had the major bleeding episode. He had preprocedural HP (platelet transfusion) and underwent snare polypectomy with electrocautery of an 18-mm tubular adenoma without procedural bleeding; however, 6 days later he experienced haematochezia, and his haemoglobin level decreased from 12 g/dL to 6.8 g/dL. Bleeding was managed with repeat colonoscopy, epinephrine injection, haemoclip placement and EACA (3 g orally every 6 hours for 10 days). Of the 10 minor bleeding complications, 8 were procedural; 2, delayed. The endoscopists' descriptions of the minor procedural bleeding instances were as follows: minor; self-limited, minimal oozing; not excessive; self-limited, small amount of bleeding; small haematoma at biopsy site; minimal.

3.4 | Bleeding complications in patients who received preprocedural HP

In our series, preprocedural HP was given to patients for 86 colonoscopy procedures. Of these, 49 (57%) procedures did not require intervention, and there were no bleeding complications. One patient with severe HA was prescribed home-infusion HP, and his colonoscopy was scheduled to coincide with the day of his prophylactic infusion. Interventions were required in 37 procedures: biopsy (9 [24%]), polypectomy (27 [73%]) and APC of an arteriovenous malformation (1 [3%]).

3.4.1 | Biopsy outcomes

Minor bleeding occurred in two of nine patients (22%) undergoing biopsy, one procedural and one delayed (Table 3). The procedural bleeding episode (small biopsy site haematoma after rectal mucosal biopsy) occurred in a 77-year-old man with AVWS, despite his receiving preprocedural IV DDAVP; he received von Willebrand factor (VWF) concentrate the next day. The second patient, a 26-year-old woman who was a symptomatic carrier of HA, received preprocedural intranasal DDAVP for multiple mucosal biopsies performed for evaluation of diarrhoea. No postprocedural HP was administered. One day after the procedure, the patient experienced haematochezia, for which she self-treated with intranasal DDAVP. The severity of bleeding was not documented in the health record.

3.4.2 | Polypectomy outcomes

In our series, six of 27 (22%) patients who had HP experienced bleeding complications after polypectomy: four procedural and two delayed (Table 3). The procedural bleeding occurred in one patient with VWD (10-mm polyp) that required placement of a haemoclip to control oozing; one patient with mild HA (cold-snare excision of a diminutive polyp); one patient with severe HA (7-mm polyp); and one patient with an unspecified platelet procoagulant defect (biopsy and fulguration of a 5-mm polyp) who received 1 g of EACA orally every 6 hours for 5 days. Of the two patients who had delayed bleeding, one with Glanzmann thrombasthenia (major bleeding) was described above; the other patient was a 64-year-old man with type 1 VWD who received preprocedural HP with VWF but no postprocedural HP. The bleeding complication occurred 9 days after sessile polypectomy and was managed with VWF concentrate and EACA (1 g orally every 6 hours for 10 days). However, importantly, none of the bleeding episodes occurred during or immediately after the intervention.

3.5 | Bleeding complications in patients who did not receive preprocedural HP

Preprocedural HP was not given for 55 procedures. Of the 55 procedures, 6 (11%) required postprocedural HP, and 26 (47%) were not associated with an intervention, did not require postprocedural HP, and were not complicated by bleeding. Of the 29 procedures that included an intervention, the interventions were biopsy in 6 (21%), polypectomy in 21 (72%), and APC of an arteriovenous malformation in 2 (7%).

3.5.1 | Biopsy outcomes

Procedural bleeding occurred after one of six biopsies. The patient who experienced bleeding was a 70-year-old man with mild HA who underwent biopsy of an ulcerated rectal mass. The bleeding was not excessive and did not require intervention. Of the five patients who did not experience bleeding, 4 (1 each with type 3 VWD, AVWS and factors VII and XI deficiency) did not receive postprocedural HP (Tables 4 and 5); one patient with mild HA received IV DDAVP.

TABLE 3 Bleeding complications categorized by timing and severity

Intervention	Total	Procedural	Immediate postprocedural	Delayed
HP (86 procedures, 37[a] interventions)				
Biopsy (n = 9)				
Major bleeding	0	0	0	0
Minor bleeding	2	1[b]	0	1
Polypectomy (n = 27)				
Major bleeding	1	0	0	1
Minor bleeding	5	4	0	1
No HP (55 procedures, 29 interventions)				
Biopsy (n = 6)				
Major bleeding	0	0	0	0
Minor bleeding	1	1	0	0
Polypectomy (n = 21)				
Major bleeding	0	0	0	0
Minor bleeding	2	2[c]	0	0

Note: Haemostatic prophylaxis (HP): 1, argon plasma coagulation (n = 1); 2, electrocautery; 3, haemoclip placed in one patient.

[a]Argon plasma coagulation, one patient.

[b]Electrocautery.

[c]Haemoclip, one patient.

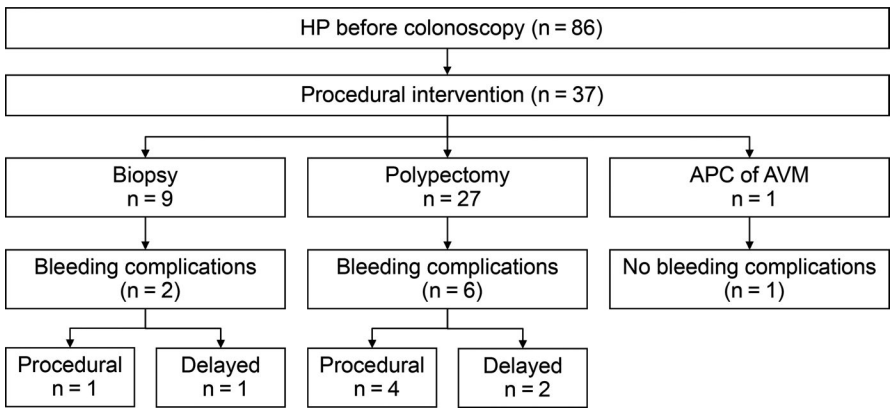

FIGURE 1 Outcomes for patients who received preprocedural haemostatic prophylaxis for colonoscopy. APC indicates argon plasma coagulation; AVM, arteriovenous malformation; HP, haemostatic prophylaxis

3.5.2 | Polypectomy outcomes

Of 21 polypectomies, two were associated with procedural bleeding. A 53-year-old man with a history of mild HA who underwent polyp biopsy and fulguration of four polyps (the largest measuring 10 mm) had minor bleeding (described as oozing), managed with postprocedural HP (recombinant factor VIII [rFVIII] and 1 g EACA orally every 6 hours for 7 days). The second patient was a 75-year-old man with mild HA who underwent snare polypectomy of three tubular adenomas (the largest measuring 8 mm); he required electrocautery to control minor bleeding but received no postprocedural HP. Of the 19 polypectomies not associated with bleeding complications, postprocedural HP was given in four cases, and 15 did not require postprocedure HP (Figure 2). As shown in Table 4, most of these procedures were performed on patients with a mild underlying bleeding disorder.

3.6 | Influence of disease severity on periprocedure management

We analysed the impact of disease severity on indications for colonoscopy, influence on HP and interventions. We based our categorization of mild vs severe bleeding disorders as described in demographic information. Analysis of differences in indications for colonoscopy, based on severity of disease, showed that a higher proportion of patients with mild bleeding disorders underwent colonoscopy for screening (31/109, 28%) than those with severe bleeding disorders (2/32, 6%; 2-sided Fisher's exact test, $P = .008$; Table 6). Age did not seem to be a variable in this difference because the median (range) age of PWBD with mild disorders and severe disorders was 59 years (3-87 years) and 66 years (6-86 years), respectively. Other indications were similar in the two groups (Table 2). Severity of bleeding disorders also did not appear to have a major

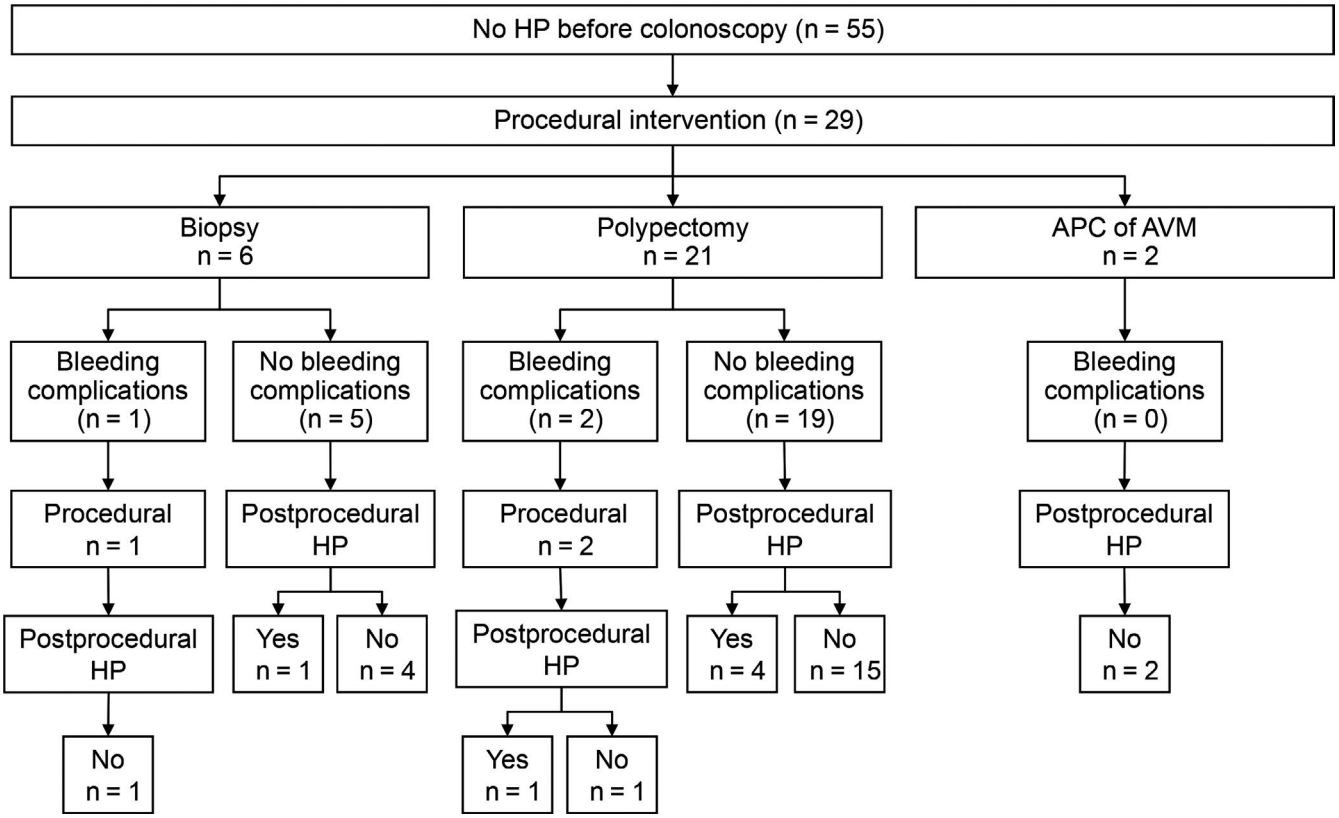

FIGURE 2 Outcomes for patients who did not receive preprocedural haemostatic prophylaxis for colonoscopy. APC indicates argon plasma coagulation; AVM, arteriovenous malformation; HP, haemostatic prophylaxis

role in the decision to use HP, which was given in 61% (66/109) of the procedures for patients with mild disorders and in 61% (20/32) of the procedures for patients with severe disorders (2-sided Fisher's exact test, $P = 1.00$). Finally, analysis of the interventions performed showed that cold-snare polypectomy was most commonly used in cases of mild bleeding disorders (10/37, 27%), whereas electrocautery was used for polypectomy in cases of severe bleeding disorders (4/9, 44%). However, this analysis is limited by the smaller total numbers of patients with severe bleeding disorders and precludes meaningful statistical analysis.

4 | DISCUSSION

To our knowledge, our study is the largest series to date to describe outcomes of periprocedural management strategies for colonoscopy in PWBD and may help to guide periprocedural HP recommendations and/or future studies. During 75 of 141 (53%) colonoscopy procedures in our study, no intervention was performed, findings that are similar to those of others, which are described in detail in the next paragraph.[8-10] We therefore speculate that, based on the ATHN report, approximately half of the 12 000 expected colonoscopies over the next decade may not result in an intervention. Bleeding risk varies by intervention type. In the general population, risk of bleeding after mucosal biopsy is approximately 0.02%, increasing to 0.4% to 1.6% after polypectomy,[11-14] with resection of polyps of at least 10 mm considered high risk for bleeding complications.[15] Other interventions, including mucosal biopsy, are considered low risk and do not require interruption of antithrombotic agents.[15,16] Nevertheless, our overall major bleeding complication rate (0.7% [1/141]) was similar to that of the general population (0.1%-0.6%)[13] and lower than that reported previously.[8-10] Furthermore, categorization (major or minor bleeding) and timing of onset of bleeding complications (in relation to intervention) are unique features of our study. Although early onset (procedural) or immediate postprocedural bleeding might be expected in the PWBD population, our study did not support this hypothesis.

We searched MEDLINE, PubMed and EMBASE using the medical subject headings "von Willebrand disease," "hemophilia," "haemophilia," "bleeding disorders" and "colonoscopy" and reviewed all English-language articles and any pertinent references in these articles to determine other studies we could use for comparison. The literature search yielded four relevant studies. One was an abstract with insufficient details to compare to our study,[17] and three were full-length publications that we included here.[8-10] In a prospective study by Davis et al,[8] 28 PWBD (severe and mild haemophilia, 9 and 12, respectively; and moderate VWD, 5) underwent 32 endoscopic procedures, 20 of which were colonoscopy procedures; 10 of the 20 colonoscopies (50%) did not require an intervention. All patients received TXA (1 g orally every 8 hours), starting the night before the procedure and continuing for 10 days for a standard risk intervention (eg, mucosal biopsy or polypectomy < 10 mm). Additional

TABLE 4 Bleeding disorders for interventions without bleeding complications despite no pre- or postprocedural HP

Bleeding disorder by procedure (baseline factor levels, %)[a]	Largest polyp, mm	Additional precautions[b]
Biopsy (n = 4)		
Type 3 VWD (<12)[c]	NA	None
AVWS (<12)[a]	NA	None
Factor VII deficiency (21)	NA	None
Factor XI deficiency (6)	NA	None
Polypectomy (n = 15)		
AVWS (<12)[c]	3	None
Mild HA (26)[a]	15	None
Mild HA (26)[a]	10	None
Mild HA (28)	8	None
Mild HA (28)	7	None
Mild HA (23)	6	Electrocautery
Mild HA (28)	4	None
Mild HA (23)	2	None
Mild HA (28)	2	None
Mild HB (10)	3	None
Type 1 VWD (19)	6	None
Type 1 VWD (31)	4	None
Type 1 VWD (31)	4	Electrocautery
Type 2A VWD (28)	4	None
Type 2B VWD (37)	4	None

Abbreviations: AVWS, acquired von Willebrand syndrome; HA, haemophilia A; HB, haemophilia B; HP, haemostatic prophylaxis; NA, not applicable; VWD, von Willebrand disease.

[a]Baseline factor levels provided for patients with VWD are ristocetin cofactor activity levels. Others are the coagulation factor activity levels appropriate for the bleeding disorder.

[b]Additional precautions included haemoclips and epinephrine injections.

[c]Procedures for patients with high-risk bleeding disorders or involving high-risk interventions.

coagulation factor replacement was given for high-risk procedures (eg, polypectomy > 10 mm). Most patients were already receiving prophylactic factor infusions as part of clinical care and therefore self-infused before their procedure.[8] Tintillier et al[9] retrospectively studied 27 patients with haemophilia who underwent 33 colonoscopy procedures; all patients received preprocedural prophylactic infusion of factor concentrates; 5 (15%) had no intervention and therefore did not receive postprocedural factor infusions. In the third study by Tomaszewski et al,[10] which was also retrospective, 48 PWBD underwent 50 colonoscopy procedures; preprocedural HP was used for all procedures, with additional postprocedural infusions for those who underwent high-risk interventions. Intervention was not required in 36% (18/50) of procedures.

The primary end point of bleeding onset reported by Tomaszewski et al[10] was 72 hours after the procedure, whereas in the reports of Davis et al[8] and Tintillier et al,[9] postpolypectomy bleeding occurred 1 to 12 days after the procedure. None of the procedures in patients who received preprocedural HP in our study were complicated by major procedural or immediate postprocedural bleeding. Minor procedural bleeding was managed with local hemostasis. The one major bleeding event occurred 6 days after the procedure in a patient with Glanzmann thrombasthenia, despite preprocedural HP. The patient safely underwent a subsequent polypectomy without preprocedural HP but with optimal local hemostasis and postprocedural platelet transfusion to prevent bleeding (Table 5). Importantly, of those not receiving preprocedural HP, the minor procedural bleeding complications were managed with local measures or postprocedural HP, or both. There were no delayed or major bleeding complications in patients who did not receive preprocedural HP.

A large proportion of procedures for the patients in our study were ordered by non-HTC providers, which was an unexpected finding. Despite efforts to educate patients or to implement alerts about the bleeding disorder in the electronic health record, these patients did not consistently inform the non-HTC ordering providers of their bleeding disorder and, thus, HTC was not consistently contacted before the procedures. As a result, many of these patients did not receive preprocedural HP. This allowed us to report outcomes for patients who did not receive preprocedural HP.

Historically, PWBD have been considered high risk for colonoscopy regardless of whether an intervention is planned, and most PWBD routinely receive preprocedural HP because bleeding rates after biopsy and polypectomy are higher than that of the general

TABLE 5 Characteristics of high-risk bleeding disorders by intervention[a,b]

Diagnosis (factor levels, %)	Procedures	Patient age	Intervention	Preprocedural HP	Postprocedural HP	Bleeding complications
Biopsy						
Dysfibrinogenemia (Cl: 44 mg/dL, PT: 438 mg/dL)	1	54	Random mucosal biopsies	Cryoprecipitate	Cryoprecipitate + 2 g EACA every 6 h for 2 wk	None
Hermansky-Pudlak syndrome	1	53	Random mucosal biopsies	DDAVP	None	None
AVWS: (<12)	1	77	Rectal mucosal biopsy	DDAVP	VWF concentrate	Procedural bleeding described as small haematoma at biopsy site
Type 3 VWD: (<12)	1	64	Mucosal biopsies	None	None	None
	2	66	Mucosal biopsy, dilation of anastomosis, injection of triamcinolone	VWF concentrate	2 g EACA every 6 h for 7 d	None
Polypectomy						
Glanzmann thrombasthenia	1	43	None	None	None	None
	2	49	Polypectomy with electrocautery	Irradiated apheresis platelet concentrate	None	Major delayed bleeding requiring hospitalization
	3	52	Polypectomy	No	Prophylactic haemoclip + 1 g EACA every 8 h for 10 d	None
	4	55	Polypectomy × 3	Irradiated apheresis platelet concentrate	Prophylactic haemoclip + 1 unit platelets + 3 g EACA every 8 h for 4 d	None
Severe HA: (<1)	1	51	Polypectomy	rFVIII	None	None
	2	53	Polypectomy	rFVIII	None	Minimal procedural bleeding
Platelet procoagulant defect	1	67	Polyp biopsy with fulguration	Platelets + DDAVP	1 g EACA every 6 h for 5 d	Small amount of self-limited procedural bleeding
	2	70	Polyp biopsy and cauterization	DDAVP	1 g EACA every 6 h for 5 d	None
AVWS: (<12)	1	49	Polypectomy	None	None	None
	2	52	APC of AVM	None	None	None
	3	52	APC of AVM	None	None	None
	4	52	Mucosal biopsies	None	None	None
Biopsy and polypectomy						
Severe HA	1	38	Mucosal biopsy and polypectomy	PD FVIII	1 g EACA every 6 h for 10 d	None

Abbreviations: APC, argon plasma coagulation; AVM, arteriovenous malformation; AVWS, acquired von Willebrand syndrome; Cl, Clauss fibrinogen; DDAVP, desmopressin acetate; EACA, epsilon aminocaproic acid; FVIII, factor VIII; HA, haemophilia A; HP, haemostatic prophylaxis; PD FVIII, plasma-derived factor VIII; PT, prothrombin time; rFVIII, recombinant factor VIII; VWD, von Willebrand disease; VWF, von Willebrand factor.

[a]Haemostatic prophylaxis or haemostatic clip.

[b]Baseline factor levels provided for VWD patients are ristocetin cofactor activity levels. Others are the coagulation factor activity levels appropriate for the underlying bleeding disorder.

TABLE 6 Differences in groups with and without preprocedure haemostatic prophylaxis

	Preprocedure haemostatic prophylaxis			No preprocedure haemostatic prophylaxis		
Disease severity	No. pts/No. colonoscopies (mean baseline [range] factor levels)[a]	Indications for colonoscopy (no.)	Interventions (no.), maximum polyp size[b]	No. pts/no. colonoscopies (mean baseline [range] factor levels)[a]	Indications for colonoscopy (no.)	Interventions (no.), maximum polyp size[b]
Patients with mild bleeding disorders						
Mild HA and symptomatic HA carriers	10/16[c] (21 [9-36])	Polyp f/u (7); screening (5); GI bleeding (2); diarrhoea (1); IDA (1)	None (9); mucosal biopsy (1); polypectomy (6): cold snare, electrocautery, epinephrine injection; 4 mm	4/15 (25 [20-28])	Polyp f/u (7); screening (2); GI bleeding (1); diarrhoea (1); IDA (1); colon ca f/u (3)	None (3); biopsy of nodule (1); biopsy of mass (1); polypectomy (10): cold snare, hot biopsy, electrocautery, fulguration; 15 mm
Moderate HA	2/4[c] (4 and 5)	Polyp f/u (1); GI bleeding (3)	None (3); polypectomy (1): cold and hot forceps; 5 mm			
Mild HB	4/6[d] (19 [13-23])	Polyp f/u (2); screening (1); GI bleeding (1); anaemia (2)	None (2); polypectomy (4): cold snare and hot biopsy forceps; 15 mm	2/2 (10 and 23)	Screening (2)	Polypectomy (2): hot biopsy and cold snare; 5 mm
Moderate HB	1/1[d] (4)	f/u of abnormal CT scan	None (1)			
Factor XI deficiency	1/1 (45)[e]	IDA (1)	None (1)	4/6 (16 [6-45])	Screening (2); diarrhoea (1); polyp f/u (1); IDA (2)	None (4); mucosal biopsy (1); polypectomy (1): cold biopsy forceps; 2 mm
VWD, type 1 (%)	15/24[f] (75/32/36)	Polyp f/u (6); screening (9); GI bleeding (8); diarrhoea (1)	None (15); APC (1); mucosal biopsy (1); polypectomy (7): cold snare, electrocautery, hot biopsy; 20 mm	8/13 (63/25/34)	Polyp f/u (4); screening (7); IDA (1); abdominal pain (1)	None (9); polypectomy (4): hot biopsy, cold snare, hot biopsy; electrocautery; 20 mm
VWD, type 2A (%)	2/4[f] (104/<12 and 28/42)	Polyp f/u (1); screening (2); GI bleeding (1)	None (3); polypectomy (1): electrocautery and snare; 5 mm	1/1 (83/28/53)	Polyp f/u (1)	Polypectomy (1): cold biopsy forceps; 4 mm
VWD, type 2B (%)	3/5[g] (83/36/59)	Screening (1); GI bleeding (4)	None (4); rectal biopsy (1)	2/2 (93/44/64)	GI bleeding (2)	None (1); polypectomy (1): cold snare; 4 mm
VWD, type 2M (%)	1/4[f] (117/28/44)	GI bleeding (2); IDA (1); colon ca f/u (1)	None (3); biopsy of mass (1)	1/1 (117/28/44)	Colon ca f/u (1)	None
Factor VII deficiency (%)	1/1[h] (40)	UC f/u	Mucosal biopsy (1)	2/2 (21 and 40)	Diarrhoea (1); UC f/u (1)	None (1); mucosal biopsy (1)
Factor II deficiency				1/1 (5)	Abnormal imaging on CT scan of abdomen	None (1)
Patients with severe bleeding disorders						
Severe HA	3/6[i] (<1)	Polyp f/u (2); GI bleeding (2); diarrhoea (1); abnormal abdominal CT scan (1)	None (3); polypectomy (2): cold biopsy forceps, electrocautery, mucosal biopsy and polypectomy (1); 10 mm			

(Continues)

TABLE 6 (Continued)

Disease severity	Preprocedure haemostatic prophylaxis			No preprocedure haemostatic prophylaxis		
	No. pts/No. colonoscopies (mean baseline [range] factor levels)[a]	Indications for colonoscopy (no.)	Interventions (no.), maximum polyp size[b]	No. pts/no. colonoscopies (mean baseline [range] factor levels)[a]	Indications for colonoscopy (no.)	Interventions (no.), maximum polyp size[b]
Severe HA with inhibitor	1/1[j]	Abnormal virtual colonoscopy	Polypectomy (1): cold snare; 5 mm			
VWD type 3	3/4[g] (19/<12/7)	GI bleeding (2); Crohn disease f/u (2)	None (3); mucosal biopsy (1)	1/2 (6/<12/8)	Crohn disease f/u (2)	None (1); mucosal biopsy (1)
AVWS	1/1[k] (126/34/35)	IDA (1)	Mucosal biopsy (1)	3/7 (21/<12/13)	GI bleeding (2); anaemia (5)	None (3); APC of AVM (2); polypectomy (1): hot biopsy; 3 mm; rectal mucosal biopsy (1)
Dysfibrinogenemia	1/1[l] (Cl 44 mg/dL; PT fib 438 mg/dL)	Diarrhoea	Mucosal biopsy (1)			
Glanzmann thrombasthenia	1/2[m]	Polyp f/u (2)	Polypectomy (2): cold biopsy forceps electrocautery, epinephrine injection, haemoclip; 18 mm	1/2	Polyp f/u (2)	None (1); polypectomy (1): cold snare, epinephrine injection, haemoclip; 10 mm
Platelet procoagulant defect	1/2[n]	Polyp f/u	Polypectomy (2): hot forceps, cauterization, fulguration; 5 mm	1/1	Diarrhoea	None
Hermansky-Pudlak syndrome	1/3[o]	Screening (2); diarrhoea (1)	None (2); mucosal biopsy (1)			

Abbreviations: APC, argon plasma coagulation; AVM, arteriovenous malformation; AVWS, acquired von Willebrand syndrome; ca, cancer; Cl, Clauss fibrinogen assay; CT, computed tomography; DDAVP, desmopressin; f/u, follow-up; GI, gastrointestinal; HA, haemophilia A; HB, haemophilia B; IDA, iron deficiency anaemia; No., number; PT, prothrombin time; PT fib, PT-derived fibrinogen; pts, patients; UC, ulcerative colitis; VWD, von Willebrand disease; VWF, von Willebrand factor.

[a]Data for patients with VWD represent mean levels of factor VIII, ristocetin cofactor activity, and VWF antigen, (%) unless otherwise indicated.

[b]The listed intervention indicates the method of polypectomy. Each method is listed once, although it may have been used more than once during multiple procedures. During each colonoscopy, more than 1 polyp may have been removed; dimensions are listed only for the largest polyp.

[c]Plasma-derived or recombinant factor VIII or intravenous DDAVP.

[d]Recombinant factor IX concentrate and prophylactic haemoclip.

[e]Fresh-frozen plasma.

[f]VWF concentrate for 2 procedures and intravenous DDAVP for 2 procedures.

[g]Plasma-derived VWF concentrate.

[h]Tranexamic acid.

[i]Recombinant or plasma-derived factor VIII concentrates.

[j]Activated prothrombin complex concentrates.

[k]Intravenous DDAVP.

[l]Cryoprecipitate.

[m]Platelets, haemoclip, postprocedure platelets and ε aminocaproic acid for major haemorrhage (described in text).

[n]Platelets and intravenous DDAVP.

[o]Intravenous DDAVP.

population despite preprocedural HP. However, our results showed that PWBD who experienced bleeding complications usually had some additive high-risk component (severe bleeding disorder or high-risk intervention). Eight of 11 (73%) bleeding complications in our series occurred after polypectomy: two after excision of moderate-sized polyps (7 mm and 8 mm), 3 after excision of large polyps (≥10 mm) and 3 in patients with severe inherited bleeding disorder (Glanzmann thrombasthenia, platelet procoagulant defect and severe haemophilia). In contrast, patients who did not have periprocedural HP or bleeding complications generally had mild bleeding disorders or smaller polyps excised.

Our data suggest that patients with mild inherited bleeding disorders may undergo colonoscopy without preprocedure HP if there is a low likelihood of intervention or a high likelihood of only a low-risk intervention. The same cannot be said about patients with severe bleeding disorders or moderate haemophilia given the small number of such patients in our cohort, which precludes meaningful conclusions regarding their need for periprocedural HP. Although we cannot necessarily predict the need for an intervention before a procedure, an alternative is to stratify likelihood by colonoscopy indication. In our series, 63% of patients undergoing colonoscopy for follow-up of polyps had an intervention, whereas less than 30% of colonoscopy procedures performed for initial colorectal cancer screening or evaluation of gastrointestinal bleeding were associated with an intervention. Additionally, 89% of those with diarrhoea had an intervention, but these were largely low-risk mucosal biopsies. For those with severe bleeding disorders and a high likelihood of polypectomy or other high-risk intervention, preprocedural HP is necessary. The type and duration of postprocedural HP will vary depending on the type of intervention.

Our study had limitations, including its retrospective nature, which caused us to rely on documentation in the electronic health record. In addition, periprocedural management was not standardized; thus, decisions on HP were made at the discretion of the ordering providers. There is generally a bias to provide preprocedural HP for more severe bleeding disorders, although our data did not demonstrate this bias, and the small numbers of such patients in our cohort preclude meaningful statistical analysis. Furthermore, because most patients had mild bleeding disorders and underwent mainly low-risk interventions, our study lacks data on outcomes of more severe bleeding disorders and high-risk interventions[15] other than for resection of polyps of at least 10 mm, for which HP should always be given. An additional limitation is the redundancy of multiple patients undergoing more than one procedure. Finally, a meaningful statistical analysis comparing outcomes of patients who did or did not receive HP based on severity of bleeding disorder was not possible because of the heterogeneity of bleeding disorders and low number of bleeding events.

In conclusion, our study showed that patients with mild bleeding disorders may potentially safely undergo colonoscopy without preprocedural HP, as long as high-risk interventions are not planned. However, additional studies are needed of patients with moderate and severe bleeding disorders. Because more than half of colonoscopy procedures do not require interventions, this approach has major cost-saving implications. This potential cost savings may be negated if the required intervention is not performed and a repeat colonoscopy with HP is required. However, centres that use this strategy should have resources available to rapidly administer postprocedural HP if a high-risk intervention is performed. In addition, we provided preliminary evidence that it is safe for experienced centres to withhold preprocedural HP for some mild bleeding disorders and low-risk interventions, as long as meticulous technique and optimal local hemostasis efforts are used. More large retrospective and prospective studies are needed to further elucidate optimal evidence-based periprocedural HP strategies for PWBD undergoing colonoscopy.

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