Management and Outcomes of Bleeding Within 30 Days of Colonic Polypectomy in a Large, Real-Life, Multicenter Cohort Study

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This article has an accompanying continuing medical education activity, also eligible for MOC credit, on page e36. Learning Objective–Upon completion of this activity, successful learners will be able to identify risk factors predicting need for therapeutic intervention in delayed post-polypectomy bleeding (DPPB); use a nomogram to estimate risk of identifying active bleeding during colonoscopy in DPPB and determine which patients could be managed conservatively; list 3 risk factors for identifying active bleeding at time of colonoscopy for DPPB; and list the most common endoscopic findings when a bleeding point is identified at the time of colonoscopy for DPPB.

BACKGROUND & AIMS: **Management of delayed (within 30 days) postpolypectomy bleeding (DPPB) has not been standardized. Patients often undergo colonoscopies that do not provide any benefit. We aimed to identify factors associated with therapeutic intervention and active bleeding after DPPB.**

METHODS: **We performed a retrospective study of 548 patients with bleeding within 30 days after an index polypectomy (DPPB; 71.9% underwent colonoscopy, 2.6% underwent primary angiographic embolization, and 25.5% were managed without intervention) at 6 tertiary centers in Spain, from January 2010 through September 2018. We collected demographic and medical data from patients. The primary outcomes were the need for therapeutic intervention and the presence of active bleeding during colonoscopy.**

RESULTS: **A need for therapeutic intervention was associated independently with the use of antithrombotic agents, hemoglobin decrease greater than 2 g/dL, hemodynamic instability, and comorbidities ($P < .05$). The bleeding point during colonoscopy was identified in 344 patients; 74 of these patients (21.5%) had active bleeding. Active use of anticoagulants (odds ratio [OR], 2.6; 95% CI, 1.5–4.5), left-sided polyps (OR, 1.95; 95% CI, 1–3.8), prior use of electrocautery (OR, 2.6; 95% CI, 1.1–6.1), and pedunculated polyp morphology (OR, 1.8, 95% CI, 1–3.2) significantly increased the risk of encountering active bleeding. We developed a visual nomogram to estimate the risk of active bleeding. Overall, 43% of the cohort did not require any hemostatic therapy. Rebleeding (<6%) and transfusion requirements were low in those managed without intervention.**

CONCLUSIONS: **In a study of patients with DPPB, we found that almost half do not warrant any therapeutic intervention. Colonoscopy often is overused for patients with DPPB. We identified independent risk factors for active bleeding that might be used to identify patients most likely to benefit from colonoscopy.**

Keywords: Gastrointestinal Hemorrhage; Colorectal Neoplasms; Endoscopy; Adverse Event.

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Abbreviations used in this paper: ASA, American Society of Anesthesiologists physical status classification; AUROC, area under the receiver operator curve; DPPB, delayed postpolypectomy bleeding; PPB, post-polypectomy bleeding.

Most current article

1542-3565/$36.00
https://doi.org/10.1016/j.cgh.2020.03.068

Polypectomy of colonic adenoma prevents death from colorectal cancer and has become the most common therapeutic endoscopic procedure worldwide.[1] Postpolypectomy bleeding (PPB) is the most frequent adverse event of the technique.[2] Most research in this field has focused on elucidating the risk factors for delayed PPB (DPPB) and exploring the benefits of prophylactic therapies. Several studies have shown that the risk of DPPB depends on variables such as polyp size and location, comorbidity, and the use of antithrombotic drugs, and can be as high as 40% in high-risk lesions.[3,4] Hemoclips to prevent DPPB may be beneficial in large lesions located in the right colon, although the debate remains open owing to conflicting results in recent clinical trials.[5–7]

Conversely, few studies have addressed the management of DPPB once patients present to the emergency department, and no evidence-based guidelines are available. Most studies represent single-center experiences with small sample sizes or have focused on wide-field endoscopic mucosal resection.[8–11] In contrast to other sources of lower gastrointestinal bleeding, the indication for colonoscopy in DPPB is merely therapeutic because the source of bleeding is known beforehand. The benefit of a therapeutic intervention is debatable in many patients, considering that a significant proportion of cases are self-limited or do not present with stigmata of recent bleeding when a colonoscopy is performed. A decision tree modeling study estimated that a repeat colonoscopy is beneficial in only 22% of patients.[12] Hence, identification of the risk factors for the need for therapeutic intervention may help physicians to select the best candidates for an invasive procedure. Likewise, it is important to identify which patients are likely to have active bleeding at a postpolypectomy site so that they can undergo colonoscopy and achieve early hemostasis. This would lead to a reduction in unnecessary endoscopic procedures, costs, and iatrogenic adverse events.

This study represents a large cohort of patients with DPPB and aims to elucidate factors associated with therapeutic intervention and active bleeding during colonoscopy for patients with DPPB. Secondarily, we aimed to evaluate the rate and predictors of rebleeding.

What You Need to Know

Background

Management of delayed postpolypectomy bleeding (DPPB) has not been standardized. Patients often undergo colonoscopies that do not provide any benefit.

Findings

In a study of patients with bleeding within DPPB, we found that almost half do not warrant any therapeutic intervention. We identified independent risk factors for active bleeding that might be used to identify patients most likely to benefit from colonoscopy.

Implications for patient care

Colonoscopy often is overused for patients with DPPB. Patients should undergo a colonoscopy examination only if they have multiple risk factors for recurrent bleeding.

Methods

Study Design and Definitions

This was an observational, multicenter, retrospective study conducted at 6 Spanish tertiary centers that provide universal public health care assistance to an area with a population of 3.1 million people. The study was performed according to the Strengthening the Reporting of Observational Studies in Epidemiology statement.[13] All patients older than age 18 years with DPPB during the first 30 days after the index polypectomy were included. An index colonoscopy (ie, colonoscopy in which a polypectomy was performed) at another institution was an exclusion criterion. The inclusion period was from January 2010 to September 2018.

DPPB was defined as any bleeding occurring after the completion of the index colonoscopy requiring emergency room presentation, hospitalization, or reintervention (repeat endoscopy, angiography, or surgery).[10] A polyp was deemed responsible for DPPB if only 1 polyp was removed at the index colonoscopy or if active bleeding was encountered at the polyp scar. If these requisites were not fulfilled, a polyp was analyzed as responsible for DPPB when it met any of the following criteria: (1) it was the largest polyp removed; (2) intraprocedural bleeding occurred during the index polypectomy; or (3) there was a single pedunculated polyp larger than 10 mm.

Rebleeding was defined as follows: (1) a new episode of hematochezia or rectorrhagia after hospital discharge; (2) a decrease in the hemoglobin count greater than 3 g/dL, additional transfusion requirements 48 hours after the therapeutic intervention, or emergency department admission in patients managed without intervention; or (3) direct visualization of active bleeding at the previously treated lesion on repeat endoscopy or angiographic embolization.[8] The study protocol adhered to the Declaration of Helsinki and was approved by the ethics committees for clinical research of the participating centers (institutional review board code: HCB/2018/0795; date: December 21, 2018). Informed consent for colonoscopy was obtained in all cases. The ethics committees waived the need for individual informed consent for study participation because of the retrospective design.

Data Collection

In-hospital, emergency department, and primary health care databases were reviewed retrospectively at the participating centers. A study-specific electronic case report form was designed and approved by the investigators before the study outset. Data were collected using the Spanish Gastroenterology Association Research electronic data capture tool.[14]

Baseline data included age, sex, comorbidities as ordinal variables (American Society of Anesthesiologists physical status classification [ASA]) and binary variables (diabetes mellitus, hypertension, chronic heart failure, chronic kidney disease [defined as a glomerular filtration rate $<$ 60 mL/min], and cirrhosis), and hemoglobin. The date, number of polypectomies, characteristics of the polyp responsible for DPPB, intraprocedural bleeding, use of hemoclips, and histology were retrieved from the index colonoscopy. Regarding the DPPB episode, we recorded the date, clinical parameters (hemodynamic instability, defined as a heart rate $>$100/minute or systolic blood pressure $<$100 mm Hg,[10] and history of syncope), and laboratory parameters at admission, active use of antiplatelets and anticoagulants upon arrival at the emergency department (defined as $<$5 days from the last intake for antiplatelets and vitamin K antagonists, $<$24 hours for low-molecular-weight heparin, and $<$48 hours for direct oral anticoagulants [$<$72 hours if renal clearance was $<$30 mL/min]), therapeutic interventions (colonoscopy, angiographic embolization, or surgery), severity according to the American Society for Gastrointestinal Endoscopy classification,[15] transfusion requirements, intensive care unit admission, use of vasoactive drugs, length of hospitalization, 30-day rebleeding, and mortality. The American Society for Gastrointestinal Endoscopy classification is detailed in the Supplementary Methods section. Regarding therapeutic colonoscopy, we further recorded if the bleeding point was located and the status of the scar (active bleeding, visible vessel-adherent clot, and fibrin-hematin; the former as a composite variable owing to the expected interobserver variability), completeness of endoscopy, therapy, and intraprocedural hemostasis in patients with active bleeding.

Statistical Analysis

Means and SD were used for continuous variables when normally distributed, whereas median and range were calculated for skewed data. Frequency counts and percentages were used for categoric data.

Continuous data were compared using the t test. The chi-squared and the Fisher exact tests were used for categoric data. One of our aims was to develop a visual nomogram to predict the probability of active bleeding during therapeutic colonoscopy based on β coefficients from logistic regression. Only variables with a plausible pathophysiological link to the outcome of interest were considered variable candidates to minimize the risk of a type I error. The strategy to select the best logistic regression predictive model comprised the generation of all possible models from the variables showing $P < .20$ in bivariate analyses. Odds ratios with 95% CIs were calculated for the variables included in the final models. The 5 best models for the presence of active bleeding are detailed in Supplementary Table 1. The area under the receiver operator curve (AUROC) evaluated discrimination. Goodness-of-fit was assessed using the Hosmer–Lemeshow test and a calibration figure. The logistic model that aimed to predict the presence of active bleeding was validated internally by bootstrapping. All tests were 2-tailed and a P value less than .05 was considered significant. Additional statistical methods are provided in the Supplementary Methods section.

Sensitivity Analyses

First, a logistic model to identify factors associated with active bleeding was developed in the entire cohort (n = 548), hypothesizing that patients managed without intervention (n = 140) did not have active bleeding during colonoscopy. This analysis intended to evaluate if the same independent predictive variables for active bleeding were selected in the whole study population. This represents a way to address the concern that the primary logistic model was developed only in those who underwent colonoscopy and not in all patients with DPPB. Second, the need for endoscopic therapy in the presence of a visible vessel or adherent clot at the DPPB scar is controversial. We aimed to identify predictors of active bleeding or a visible vessel-adherent clot as a composite outcome.

Results

Study Population

The final population comprised 548 patients (Figure 1). The mean age was 67.7 years. DPPB occurred after a mean of 4 days, and 443 patients (80.8%) required hospitalization. At admission, 134 patients (24.5%) were receiving active treatment with platelet anti-aggregants and 160 (29.2%) with anticoagulants.

DPPB was mild in 127 patients (23.2%), moderate in 398 (72.6%), and severe in 23 (4.2%). In total, 394 patients (71.9%) underwent colonoscopy and 14 (2.6%) underwent primary angiographic embolization; 140 (25.5%) were managed without intervention. Only 1 patient with massive bleeding during colonoscopy, in whom intraprocedural hemostasis failed, required surgery (Figure 1). Polyp features, transfusion requirements, length of hospitalization, intensive care unit

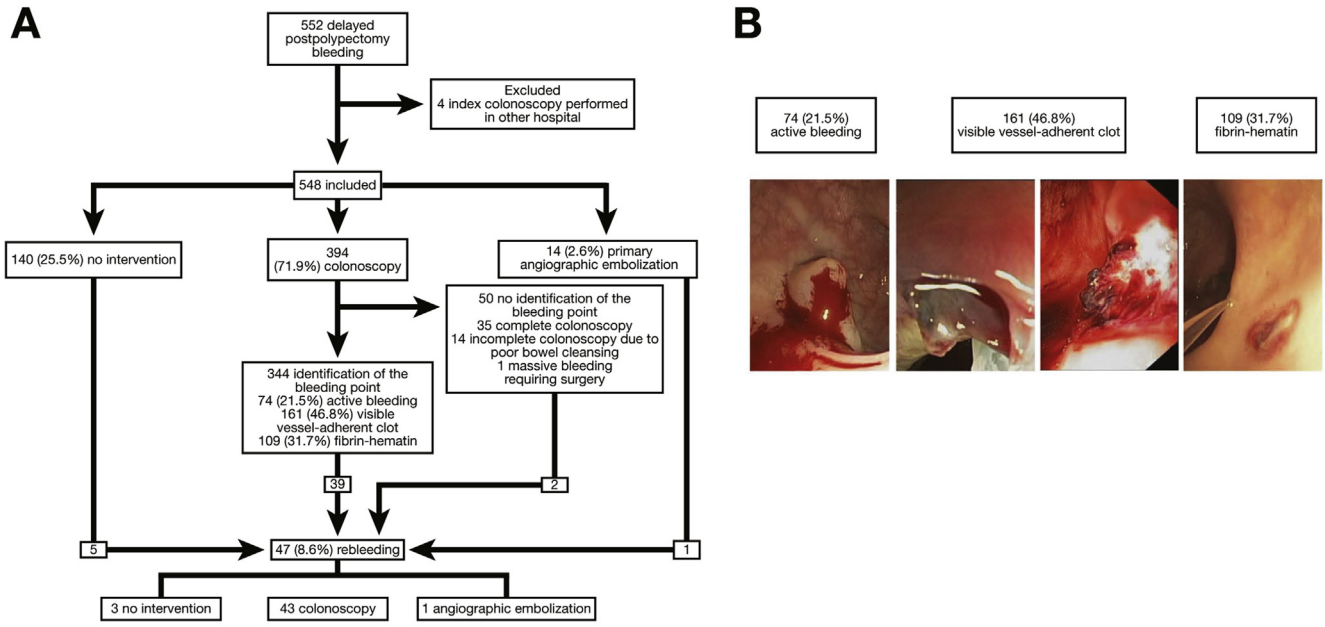

Figure 1. (*A*) Study flowchart. (*B*) Bleeding point during colonoscopy (n = 344).

admission, and clinical data are outlined further in Table 1.

Predictors of a Therapeutic Intervention and Bleeding Severity

A total of 408 patients (74.5%) were managed initially with a therapeutic intervention (ie, colonoscopy, angiographic embolization, or surgery) (Figure 1). Patients managed without intervention had lower transfusion requirements (4.3% vs 31.1%; $P < .001$). On multivariate analysis, increased comorbidity (ASA $\geq$ III), active use of platelet anti-aggregants and anticoagulants, a hemoglobin decrease of more than 2 g/dL, and hemodynamic instability were significantly more common in patients who underwent a therapeutic intervention (Table 2).

The active use of anticoagulants and platelet anti-aggregants, an ASA of III or higher, prior use of electrocautery, and hemodynamic instability at admission were associated independently with greater bleeding severity (Supplementary Table 2).

Colonoscopy Outcomes: Treatments, Intraprocedural Hemostasis, and Predictors of Active Bleeding

In total, 394 patients were managed initially by colonoscopy. The bleeding point was located in 344 (87.3%): 74 (21.5%) presented with active bleeding, 161 (46.8%) with a visible vessel-adherent clot, and 109 (31.7%) with fibrin-hematin. Endoscopic hemostatic therapy was performed in 290 (73.6%). Intraprocedural hemostasis was achieved in 73 of the 74 patients with active bleeding (98.6%; 95% CI, 92.7%–99.8%). All lesions with active bleeding, most scars with a visible vessel-adherent clot (157 of 161; 97.5%), and 54% of the ulcers with fibrin-hematin (59 of 109) received at least 1 hemostatic treatment. The reasons why patients did not receive hemostatic therapy during colonoscopy (n = 104) were as follows: 50 patients had no locatable bleeding point, 50 patients had fibrin-hematin at the polyp ulcer, and 4 patients had a visible vessel-adherent clot and the decision was based on endoscopist criteria. The endoscopic therapies are described in Supplementary Table 3. Hemoclips (68.3%) and sclerotherapy with adrenaline (43.6%) were the most common modalities.

Overall, 235 patients (42.9%) did not receive any endoscopic, angiographic, or surgical hemostatic method during the 30-day follow-up evaluation: 136 were managed without intervention, 47 had no locatable bleeding point during colonoscopy, 49 had fibrin-hematin, and 3 had a visible vessel-adherent clot. This subgroup also had low transfusion requirements compared with patients who required at least 1 hemostatic therapy (5.1% vs 38.7%; $P < .001$).

The active use of anticoagulants upon arrival at the emergency department, left-sided colon, pedunculated morphology, and hot snare polypectomy were selected for the best logistic model developed to predict the presence of active bleeding (Table 3). The AUROC in the original data set was 0.73 (95% CI, 0.67–0.80), and the estimated AUROC after bootstrapping was 0.69 (95% CI, 0.64–0.75; optimism, 0.04). Calibration was good according to the Hosmer–Lemeshow test ($P = .73$) and the calibration plot (Supplementary Figure 1). The probability of active bleeding can be estimated using the nomogram depicted in Figure 2. The number of patients

in each predicted risk category (4 risk factors, 3 risk factors, 2 risk factors, 1 risk factor, and 0 risk factors) is shown in Supplementary Table 4.

Table 1. Baseline Characteristics of the Study Population

Variable	
Patients, N	548
Age, *y*	67.7 (12.1)
Male sex	372 (67.9%)
Comorbidity	
Hypertension	292 (53.3%)
Diabetes mellitus	119 (21.7%)
Chronic heart failure	65 (11.9%)
Chronic kidney disease	38 (7%)
Cirrhosis	17 (3.1%)
Hematologic disease	7 (1.3%)
ASA scale	
I	110 (20.1%)
II	295 (53.8%)
III	136 (24.8%)
IV	7 (1.3%)
Total number of polypectomies	1798
Median polypectomies per patient (range)	2 (1–50)
Patients with 1 or more polyps >20 mm	201 (36.7%)
Index or bleeding polyp	
Median size (range), *mm*	15 (2–100)
Morphology	
Flat	127 (23.2%)
Sessile	246 (44.9%)
Pedunculated	171 (31.2%)
Missing	4 (0.7%)
Location	
Right colon	215 (39.2%)
Left colon	326 (59.5%)
Missing	7 (1.3%)
Type of polypectomy	
Cold biopsy forceps	10 (1.8%)
Cold snare	120 (21.9%)
Hot snare	418 (76.3%)
Intraprocedural bleeding	75 (13.7%)
Prophylactic hemoclips	153 (27.9%)
Histology	
Tubular adenoma	267 (48.7%)
Tubulovillous adenoma	112 (20.4%)
Villous adenoma	30 (5.5%)
Hyperplastic	26 (4.7%)
Adenocarcinoma	20 (3.6%)
Sessile serrated polyp	16 (2.9%)
Inflammatory	8 (1.5%)
Traditional serrated polyp	7 (1.3%)
Other	6 (1.1%)
Nonretrieved	56 (10.2%)
Dysplasia	
No	52 (9.5%)
Low-grade	340 (62%)
High-grade	80 (14.6%)
Invasive adenocarcinoma	20 (3.6%)
Nonretrieved	56 (10.2%)
Variables at admission	
Systolic blood pressure, *mm Hg*	128 (24)
Diastolic blood pressure, *mm Hg*	72 (14)
Heart rate, beats per minute	80 (17)
Hemoglobin decrease, *g/dL*	1.4 (1.8)
Syncope	33 (6%)
Platelets, $\times 10^3/mm^3$	215 (76.9)
International normalized ratio	1.2 (0.5)
Patients requiring transfusion, n	133 (24.3%)
Intensive care unit admission	26 (4.7%)
Use of vasoactive drugs	7 (1.3%)
Median length of hospitalization, *d* (range)	3.4 (0–35)

NOTE. Quantitative variables are expressed as means (SD) unless otherwise specified.
ASA, American Society of Anesthesiologists.

Rebleeding and Mortality

Forty-seven patients (8.6%; 95% CI, 6.5%–11.2%) rebled within the first 30 days, 25 of whom had been discharged (see clinical management in Figure 1). The rates of rebleeding stratified by type of bleeding during the index colonoscopy at the time of DPPB were 14.9% for active bleeding, 10.5% for a visible vessel-adherent clot, and 10.1% for fibrin-hematin ($P = .50$).

On multivariate analysis, patients not receiving any intervention (n = 140) had a lower rate of rebleeding than those who required an intervention (3.6% vs 10.3%) (Table 4). No other predictors of rebleeding were identified. The rate of rebleeding also was lower in patients who did not require any type of hemostatic intervention (n = 235; 5.5% vs 10.9%; univariate $P = .027$).

The only mortality concerned a 74-year-old with significant cardiopulmonary comorbidity who died of non–bleeding-related causes 15 days after achieving endoscopic hemostasis (30-day mortality, 0.18%; 95% CI, 0.03%–1.03%).

Sensitivity Analyses

The same independent predictors of active bleeding in the patients who underwent colonoscopy (n = 344) (Table 3) were selected for the best logistic model in the entire cohort (n = 548): use of anticoagulants, left-sided colon, pedunculated morphology, and hot snare polypectomy (Supplementary Table 5).

Anticoagulant therapy and left-sided colon also were associated independently with the presence of active bleeding or a visible vessel-adherent clot (Supplementary Table 6).

Discussion

DPPB management remains empiric in clinical practice. The decision to perform an invasive procedure usually is based on physician expertise or local protocols. This was a large study that aimed to identify patients with DPPB who are more likely to benefit from a

Table 2. Patients Undergoing Therapeutic Intervention (Colonoscopy, Angiographic Embolization, or Surgery) vs No Intervention

	Intervention n = 408	No intervention n = 140	Univariate *P* value	Multivariate OR (95% CI), *P* value Area under the curve, 0.71 Hosmer–Lemeshow *P* value = .38
Age, *y*	68 (12)	65 (12)	**.01**	Excluded from final model
Male sex	282 (69.1%)	90 (64.3%)	.29	
ASA comorbidity ≥ III	126 (30.9%)	17 (12.1%)	**<.01**	**2.15 (1.17–3.94), *P* = .014**
Antiplatelet therapy	115 (28.2%)	19 (13.6%)	**<.01**	**2.38 (1.35–4.21), *P* = .003**
Anticoagulant therapy	131 (32.1%)	29 (20.7%)	**.01**	**1.76 (1.05–2.97), *P* = .033**
International normalized ratio	1.21 (0.5)	1.20 (0.5)	.95	
Platelets, $\times 10^3/mm^3$	204 (61)	210 (47)	.64	
Polyp characteristics				
Size			.78	
<10 mm	99 (24.3%)	38 (27.1%)		
10–20 mm	209 (51.2%)	70 (50%)		
>20 mm	100 (24.5%)	32 (22.9%)		
Right-sided colon	159 (39%)	56 (41%)	.70	
Pedunculated	122 (31.1%)	44 (31.9%)	.87	
Type of polypectomy			.20	
Cold biopsy forceps	7 (1.7%)	3 (2.1%)		
Cold snare	82 (20.1%)	38 (27.1%)		
Hot snare polypectomy	319 (78.1%)	99 (70.7%)		
Intraprocedural bleeding	52 (12.7%)	23 (16.4%)	.30	
Previous prophylactic hemoclips	126 (30.9%)	27 (19.3%)	**.01**	1.57 (0.96–2.59), *P* = .07
Previous injection of diluted adrenaline	30 (7.4%)	15 (11%)	.21	
Previous argon plasma coagulation use	11 (2.7%)	2 (1.4%)	.53	
Previous prophylactic coagulation of submucosal vessels	7 (1.7%)	4 (2.8%)	.48	
Syncope	29 (7.1%)	4 (2.9%)	.07	Excluded from final model
Hemoglobin decrease >2 g/dL	220 (53.9%)	58 (41.4%)	**.01**	**1.63 (1.02–3.12), *P* = .043**
Hemodynamic instability	118 (28.9%)	16 (11.4%)	**< .01**	**3.15 (1.77–5.61), *P* < .001**
Days from index colonoscopy	4.1 (4)	4.3 (5.6)	.67	
Participating center, n (row %)			.57	
Hospital no. 1	137 (70.6)	57 (29.4)		
Hospital no. 2	69 (74.2)	24 (25.8)		
Hospital no. 3	37 (77.1)	11 (22.9)		
Hospital no. 4	27 (77.1)	8 (22.9)		
Hospital no. 5	44 (83)	9 (17)		
Hospital no. 6	94 (75.2)	31 (24.8)		
Patients requiring transfusion, n	127 (31.1%)	6 (4.3%)	**<.001**	Not considered for the final model
Median length of hospitalization (range)	3.9 (6)	2.4 (6)	.24	

NOTE. Quantitative variables are expressed as means (SD) unless otherwise specified. *P* values in bold are significant.
ASA, American Society of Anesthesiologists; CI, confidence interval.

therapeutic intervention. We gathered the 8-year experience of 6 tertiary centers and found that readily available variables at admission serve to estimate the risk that a lesion with active bleeding is encountered on colonoscopy. Our data suggest that a substantial number of patients can be managed without intervention with a very low risk of rebleeding.[2,10,11]

Studies that focus on the management of DPPB are mainly descriptive and suggest that invasive procedures do not always lead to a hemostatic intervention, implying that colonoscopy can be avoided in many patients. Therefore, the identification of variables that enable risk stratification of DPPB is of utmost importance to improve the management of this growing population. Here, we found that patients with active use of antithrombotics, increased comorbidity, a hemoglobin decrease of more than 2 g/dL, or hemodynamic instability were more likely to require an intervention. Only 2 studies with smaller sample sizes have addressed this issue previously. Mirroring our results, Derbyshire et al[2] found that a hemoglobin decrease of more than 2 g/dL and/or a blood transfusion can be used as markers to guide the necessity of an intervention in a study of 68 patients with DPPB. Burgess et al[10] conducted a prospective study comprising 61 patients with DPPB after wide-field endoscopic mucosal resection. They also found that increased comorbidity and transfusion were associated independently with an invasive procedure. Their prospective study provides relevant information, but there are several differences from our study that deserve further consideration. Here, all DPPB cases were included, regardless of polyp size and resection

Table 3. Factors Associated With Active Bleeding During Colonoscopy

	Active bleeding n = 74	No active bleeding n = 270	Univariate *P* value	Multivariate OR (95% CI), *P* value Area under the curve, 0.73 Hosmer–Lemeshow *P* value = .73
Age, *y*	69.6 (12.3)	68.1 (12.1)	.37	
ASA comorbidity ≥ III	28 (37.8%)	79 (29.3%)	.16	
Antiplatelet therapy	17 (23%)	73 (27%)	.48	
Anticoagulant therapy	38 (51.4%)	78 (28.9%)	**<.001**	**2.57 (1.47–4.49), *P* = .001**
Hemoglobin decrease, >2 g/dL	38 (51.4%)	110 (40.7%)	.11	
International normalized ratio	1.23 (0.54)	1.20 (0.52)	.62	
Platelets, $\times 10^3/mm^3$	208 (40)	218 (34)	.36	
Polyp characteristics				
Size			.26	
<10 mm	15 (20.3%)	71 (26.3%)		
10–20 mm	43 (58.1%)	128 (47.4%)		
>20 mm	16 (21.6%)	71 (26.3%)		
Location				
Left	54 (73%)	156 (57.8%)	**.01**	**1.95 (1.01–3.75); *P* = .046**
Right	19 (25.7%)	112 (41.5%)		Reference
Missing	1 (1.4%)	2 (0.7%)		
Morphology				
Flat-sessile	40 (54.1%)	192 (71.1%)		Reference
Pedunculated	33 (44.6%)	77 (28.5%)	**.01**	**1.76 (0.96–3.22), *P* = .069**
Missing	1 (1.4%)	1 (0.5%)		
Previous use of electrocautery				
No (cold biopsy forceps or cold snare polypectomy)	8 (24.4%)	66 (24.4%)		Reference
Yes (hot snare polypectomy)	66 (89.1%)	204 (75.6%)	**.01**	**2.60 (1.10–6.10), *P* = .028**
Histology			.56	
Tubular	42 (56.8%)	125 (46.3%)		
Adenoma with villous component	19 (25.7%)	83 (30.7%)		
Serrated	7 (9.5%)	19 (7%)		
Invasive adenocarcinoma	1 (1.4%)	7 (2.6%)		
Other	1	8 (3%)		
Nonretrieved	4 (5.4%)	28 (1.03%)		
Dysplasia			.61	
No	4 (5.4%)	23 (8.5%)		
Low-grade	49 (66.2%)	173 (64.1%)		
High-grade	15 (20.3%)	39 (14.4%)		
Invasive	2 (2.7%)	7 (2.6%)		
Nonretrieved	4 (5.4%)	38 (14.1%)		
Intraprocedural bleeding	12 (16.2%)	33 (12.2%)	.41	
Previous prophylactic hemoclips	27 (36.5%)	81 (30%)	.29	
Previous injection of diluted adrenaline	8 (11%)	20 (7.4%)	.32	
Previous argon plasma coagulation use	1 (1.4%)	7 (2.6%)	1	
Previous prophylactic coagulation of submucosal vessels	2 (2.8%)	5 (1.9%)	.64	
Participating center, n (row %)			.92	
Hospital no. 1	62 (83.8%)	12 (16.2%)		
Hospital no. 2	43 (75.4%)	14 (24.6%)		
Hospital no. 3	33 (78.6%)	9 (21.4%)		
Hospital no. 4	20 (80%)	5 (20%)		
Hospital no. 5	31 (73.8%)	11 (26.2%)		
Hospital no. 6	81 (77.9%)	23 (22.1%)		
Syncope	3 (4%)	16 (5.9%)	.77	
Hemodynamic instability	24 (32.4%)	70 (25.9%)	.27	

NOTE. Quantitative variables are expressed as means (SD). *P* values in bold are significant.
ASA, American Society of Anesthesiologists; CI, confidence interval.

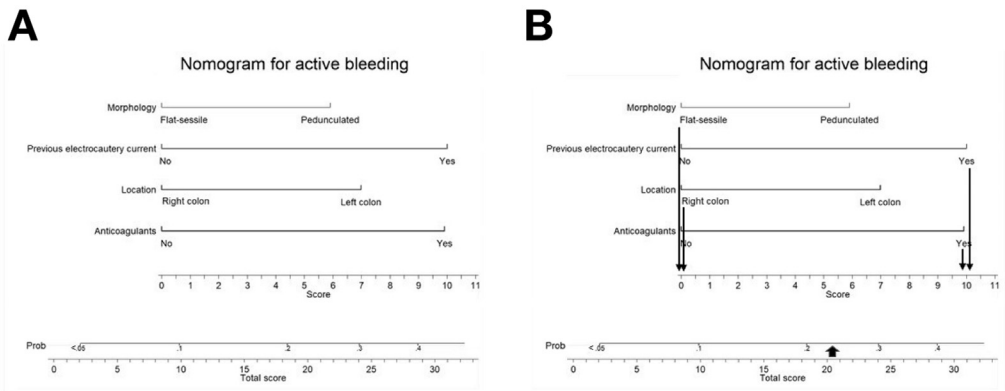

Figure 2. Nomogram for active bleeding (*A*) during colonoscopy and (*B*) graphic instructions. A patient with delayed postpolypectomy bleeding from a sessile polyp removed by hot snare polypectomy, located in the right colon, and under anticoagulant therapy has a score of 20 points. The total score translates into a probability of active bleeding of approximately 23%. Patients with the 4 risk factors have a predicted probability of active bleeding of approximately 50%, whereas patients with none have a probability of less than 5%. Prob, probability.

technique, to better represent what clinicians face in daily practice. Indeed, 58.9% of the polyps in our cohort were smaller than 2 cm and nearly 25% of the polyps were removed via cold snare polypectomy or cold biopsy forceps. In addition, both mentioned studies included variables that can occur after the outcome of interest (ie, blood transfusion), which may hamper the applicability of predictive models. We decided to include only variables that easily are available at admission, which is when the decision to perform an intervention usually is made.

The decision to perform an invasive procedure ultimately relied on the physician in charge in our cohort and in previous ones. Thus, we also aimed to identify predictors of an objective endoscopic sign that could differentiate those patients more likely to benefit from active therapy, which explains our analysis of predictors of active bleeding during colonoscopy. In contrast to gastroduodenal ulcers, in which the Forrest classification guides therapy and provides information on rebleeding risk, it is unknown which DPPB lesions require endoscopic treatment. However, it seems reasonable that scars with active bleeding would benefit from hemostatic treatment. In addition, active bleeding has low interobserver agreement,[16] which is always a concern in retrospective research. We found that pedunculated morphology, previous use of electrocautery, active use of anticoagulants at admission, and left-sided colon location all were predictors of active bleeding. The reason why pedunculated morphology is a risk factor could be the presence of a thick central vessel, whereas electrocautery is known to cause more significant damage in submucosal vessels.[17] The explanation for left-sided location remains elusive, but it also has been suggested as a potential marker of DPPB severity.[2] The nomogram depicted in Figure 2 serves to estimate the risk of active bleeding in a straightforward manner. Interestingly, a sensitivity analysis conducted in the whole study population identified the same variables as independent predictors of active bleeding. We believe that our other sensitivity analysis that parallels the Forrest IIa to IIb scenario also provides clinically relevant data. Notably, anticoagulants and a left-sided location remained independent predictors of stigmata of recent bleeding. It is vital to highlight that polyp size does not seem to influence the risk of active bleeding, the need for therapeutic intervention, or bleeding severity.[8] Similarly, prophylactic clipping did not reduce the risk that active bleeding was encountered or ameliorate bleeding severity. Consequently, these parameters should not be used to guide the management of DPPB.

Regarding endoscopic therapy, intraprocedural hemostasis was achieved in all but 1 patient and hemoclipping was the most common hemostatic method. In 2014, an electronic survey also showed that hemoclipping was the preferred method.[18] Single-arm studies have indicated that hemoclips are highly effective in achieving intraprocedural hemostasis in DPPB,[8,9,18] but no randomized trials comparing different methods are available. Careful application of hemoclips to thin-walled postpolypectomy ulcers is mandatory because cases of perforation have been reported. Sclerotherapy may help to achieve intraprocedural hemostasis but does not seem to have an impact on rebleeding and carries a risk of perforation.[8] TC-325 (Hemospray, Cook Medical, Winston-Salem, NC), which is a noncontact method, is effective in patients receiving antithrombotics and theoretically could reduce the risk of muscular damage. This agent has shown promising results in DPPB, although more data are needed.[19,20] Similarly, other noncontact hemostatic powders have shown favorable results in small case series and deserve further testing.[20]

Rebleeding occurred in 8.6% of our cohort patients, within the range of prior studies (7.6%–9.8%).[8,10] In our study, patients managed conservatively had a very low risk of rebleeding and transfusion requirements. This result has clinical implications and indicates that a

Table 4. Factors Associated With Rebleeding

	Rebleeding N = 47	No rebleeding N = 501	Univariate *P* value	Multivariate OR (95% CI), *P* value Area under the curve = 0.69 Hosmer–Lemeshow *P* value = .48
Age, *y*	68 (12)	68 (12)	.96	
ASA comorbidity ≥ III	14 (34%)	127 (25.4%)	.19	
Antiplatelet therapy	10 (21.3%)	124 (24.8%)	.59	
Anticoagulant therapy	16 (34%)	144 (33%)	.44	
International normalized ratio	1.27 (0.7)	1.2 (0.5)	.43	
Platelets, $\times 10^3/mm^3$	203 (69)	213 (43)	.44	
Polyp characteristics				
Size			.41	
<10 mm	10 (21.3%)	127 (25.3%)		
10–20 mm	22 (46.8%)	257 (51.3%)		
>20 mm	15 (31.9%)	117 (23.4%)		
Location				
Left	34 (72.3%)	292 (58.3%)		Reference
Right	13 (27.7%)	202 (40.3%)	.08	0.55 (0.28–1.08), *P* = .09
Missing	0	7 (1.4%)		
Morphology				
Flat-sessile	27 (52.6%)	346 (69.1%)		
Pedunculated	20 (47.4%)	151 (30.1%)	.09	Excluded from final model
Missing	0	4 (0.8%)		
Previous use of electrocautery				
No (cold biopsy forceps or cold snare polypectomy)	8 (17%)	121 (24.2%)		
Yes (hot snare polypectomy)	39 (83%)	380 (75.8%)	.27	
Bleeding point (n = 344)			.50	
Active bleeding	11 (28%)	63 (20.6%)		
Visible vessel-adherent clot	17 (44%)	144 (47.2%)		
Fibrin-hematin	11 (28%)	98 (32%)		
Management				
Endoscopic, angiographic, or surgical hemostatic treatment	33 (70.2%)	274 (54.7%)		Reference
Colonoscopy without hemostatic treatment	9 (19.8%)	92 (18.4%)		0.83 (0.38–1.80), *P* = .63
No therapeutic intervention	5 (10.6%)	135 (27%)	**.04**	**0.31 (0.12–0.82), *P* = .02**
No endoscopic, angiographic, or surgical hemostatic intervention	13 (27.6%)	222 (44.3%)	**.027**	Not considered for final model

NOTE. Quantitative variables are expressed as means (SD). *P* values in bold are significant.
ASA, American Society of Anesthesiologists; CI, confidence interval.

substantial number of patients with DPPB can be managed without intervention.

Other strengths of our study stem from the descriptive analysis of a large population with DPPB. No treatment was performed in 26.4% of colonoscopies, and nearly one-third did not have stigmata of recent bleeding, which suggests that colonoscopy probably was overused, as pointed out in previous cohorts.[2,10–12] Only 1 patient required surgery, a considerably lower proportion compared with initial reports of DPPB.[11,21] Furthermore, only 1 non–bleeding-related death was recorded. This represents a differential characteristic from other sources of lower gastrointestinal bleeding in which mortality can be as high as 17.8%, making DPPB a unique scenario that merits individualized management.[22]

Our study had limitations. Its retrospective design was the major limitation and implies that multivariate analyses should be validated externally in prospective research. However, the variables identified in our work are consistent with previous knowledge, cost-free, and easily accessible at admission, reinforcing our belief that our study provides new and relevant information for clinical practice. Another limitation was the highly heterogeneous endoscopic treatments used during colonoscopy, which preclude us from discerning any differences among them. Finally, the study was performed in a single country at tertiary hospitals with on-call gastroenterologists, which should be considered when our results are being extrapolated.

In conclusion, colonoscopy often is overused in DPPB. Active bleeding was found in only one fifth of

colonoscopies and nearly half of the patients with DPPB did not require any hemostatic treatment. Furthermore, we showed that patients treated without intervention had excellent outcomes in terms of rebleeding and transfusion requirements. Clinical and polyp data may help to identify the subgroup most likely to benefit from an invasive procedure. Future research should aim for better risk stratification of DPPB, elucidate the most cost-effective hemostatic method, and assess if DPPB scars without active bleeding benefit from endoscopic treatment.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2020.03.068.

References

1. Zauber AG, Winawer SJ, O'Brien MJ, et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. N Engl J Med 2012;366:687–696.
2. Derbyshire E, Hungin P, Nickerson C, et al. Post-polypectomy bleeding in the English National Health Service Bowel Cancer Screening Programme. Endoscopy 2017;49:899–908.
3. Albéniz E, Fraile M, Ibáñez B, et al. A scoring system to determine risk of delayed bleeding after endoscopic mucosal resection of large colorectal lesions. Clin Gastroenterol Hepatol 2016;14:1140–1147.
4. Jaruvongvanich V, Prasitlumkum N, Assavapongpaiboon B, et al. Risk factors for delayed colonic post-polypectomy bleeding: a systematic review and meta-analysis. Int J Colorectal Dis 2017;32:1399–1406.
5. Feagins LA, Smith AD, Kim D, et al. Efficacy of prophylactic hemoclips in prevention of delayed post-polypectomy bleeding in patients with large colonic polyps. Gastroenterology 2019;157:967–976.
6. Pohl H, Grimm IS, Moyer MT, et al. Clip closure prevents bleeding after endoscopic resection of large colon polyps in a randomized trial. Gastroenterology 2019;157:977–984.
7. Albéniz E, Álvarez MA, Espinós JC, et al. Clip closure after resection of large colorectal lesions with substantial risk of bleeding. Gastroenterology 2019;157:1213–1221.
8. Lee J-M, Kim WS, Kwak MS, et al. Clinical outcome of endoscopic management in delayed postpolypectomy bleeding. Intest Res 2017;15:221–227.
9. Parra-Blanco A, Kaminaga N, Kojima T, et al. Hemoclipping for postpolypectomy and postbiopsy colonic bleeding. Gastrointest Endosc 2000;51:37–41.
10. Burgess NG, Williams SJ, Hourigan LF, et al. A management algorithm based on delayed bleeding after wide-field endoscopic mucosal resection of large colonic lesions. Clin Gastroenterol Hepatol 2014;12:1525–1533.
11. Sorbi D, Norton I, Conio M, et al. Postpolypectomy lower GI bleeding: descriptive analysis. Gastrointest Endosc 2000;51:690–696.
12. Sonnenberg A. Management of delayed postpolypectomy bleeding: a decision analysis. Am J Gastroenterol 2012;107:339–342.
13. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol 2008;61:344–349.
14. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–381.
15. Cotton PB, Eisen GM, Aabakken L, et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. Gastrointest Endosc 2010;71:446–454.
16. Mondardini A, Barletti C, Rocca G, et al. Non-variceal upper gastrointestinal bleeding and Forrest's classification: diagnostic agreement between endoscopists from the same area. Endoscopy 1998;30:508–512.
17. Takayanagi D, Nemoto D, Isohata N, et al. Histological comparison of cold versus hot snare resections of the colorectal mucosa. Dis Colon Rectum 2018;61:964–970.
18. Feagins LA, Spechler SJ. Use of hemoclips and other measures to prevent bleeding during colonoscopy by gastroenterologists in Veterans Affairs hospitals. Am J Gastroenterol 2014;109:288–290.
19. Rodríguez de Santiago E, Burgos-Santamaria D, Pérez-Carazo L, et al. Hemostatic spray powder TC-325 for GI bleeding in a nationwide study: survival and predictors of failure via competing risks analysis. Gastrointest Endosc 2019;90:581–590.
20. Mourad FH, Leon RW. Role of hemostatic powders in the management of lower gastrointestinal bleeding: a review. J Gastroenterol Hepatol 2018;33:1445–1453.
21. Rosen L, Bub DS, Reed JF, et al. Hemorrhage following colonoscopic polypectomy. Dis Colon Rectum 1993;36:1126–1131.
22. Oakland K, Guy R, Uberoi R, et al. Acute lower GI bleeding in the UK: patient characteristics, interventions and outcomes in the first nationwide audit. Gut 2018;67:654–662.

Reprint requests

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Acknowledgments
The authors thank Santiago Ortiz Galindo, Oriol Sendino, Henry Cordova, Andres Cárdenas, Isis Araujo, Karina Chavez, Begoña González-Suárez, Gloria Fernández-Esparrach, Angels Ginés, and Josep Llach from the Endoscopic Unit at the Hospital Clinic of Barcelona. The authors also thank Kevin Clayton for English editing.

Conflicts of interest
These authors disclose the following: María Pellisé has received a research grant from Fujifilm, a consultancy fee from Norgine, speaker's fees from Norgine, Olympus, Casen Recordati, and Janssen, and an editorial fee from Thieme; and Liseth Rivero-Sánchez has received a speaker's fee from Casen Recordati. The remaining authors disclose no conflicts.

Funding
This study was funded by the Fundación Científica Asociación Española Contra el Cáncer (GCB13131592CAST), Agència de Gestió d'Ajuts Universitaris i de Recerca (2017 SGR 653), and Instituto de Salud Carlos III (FIS PI19/01050). The Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas is funded by the Instituto de Salud Carlos III. Also supported by the Fundación Científica Asociación Española Contra el Cáncer (GCB13131592CAST) and by the Agència de Gestió d'Ajuts Universitaris i de Recerca (2017 SGR 653) (L.R.S.). The Research electronic data capture tools are hosted at the Asociación Española de Gastroenterología (http://www.aegastro.es). The Asociación Española de Gastroenterología is a nonprofit scientific and medical society focused on gastroenterology and provided this service free of charge, with the sole aim of promoting independent investigator-driven research.

Supplementary Methods

Statistical Methods

Graphic plots and the Shapiro–Wilk test assessed normality. Rebleeding and intraprocedural hemostasis 95% CIs were calculated by the Wilson method.

No sample size estimation was performed for the descriptive analysis. For multivariate analysis $\alpha = .05$, and presuming 10 events per variable, a minimum of 250 required cases was estimated assuming 25% active bleeding during colonoscopy and 50% of patients requiring therapeutic intervention based on previous reports.

We aimed to develop and internally validate a predictive model using nonconditional binary logistic regression. The outcome of interest was the presence of active bleeding during colonoscopy (n = 74). Only variables with a plausible physiopathological link with the outcome of interest and readily accessible at admission were tested in bivariate analyses. The strategy to identify the best prognostic model consisted in the generation and evaluation of all possible models from all candidate variables with a *P* value less than .20 in univariate comparisons. This was accomplished with the Stata (StataCorp LLC, College Station, TX) user-command *allsets*[1] (Doménech JM, Navarro JB. Find the best subset for Linear, Logistic and Cox Regression: User-written command allsets for Stata [computer program].V1.2.4. Barcelona: Graunt21; 2018).[1] This command helps to find the best subset for linear, logistic, and Cox regression and has been used in other studies focused on gastrointestinal bleeding.[2] For logistic regression Akaike information criteria, Schwarz Bayesian criterion, the area under the curve and Hosmer–Lemeshow goodness-of-fit were computed for each subset. The Hosmer–Lemeshow goodness-of-fit test was computed using 10 quantiles to group data. We selected the best model based on these parameters and clinical applicability. The best 5 prognostic models are presented in Supplementary Table 1. Backward stepwise regression ($P = .10$ for exclusion, $P = .05$ for inclusion) selected the same final model.

The bivariate analysis included the following: age, comorbidity, active use of antithrombotics, hemoglobin decrease of more than 2 g/dL, international normalized ratio, platelet, polyp characteristics, previous treatments, previous intraprocedural bleeding, site, syncope, and hemodynamic instability at admission. Interaction terms were not considered given the lack of previous knowledge supporting clinically relevant interactions and the study sample size. Variables showing a *P* value less than .20 were considered for the maximum model and entered in the allsets command. Afterward, the allsets command was run in Stata. Goodness-of-fit was assessed using the Hosmer–Lemeshow test and calibration plots that plotted observed against predicted risk. The AUROC was calculated to evaluate the discriminative ability of the logistic models. The linearity of quantitative independent variables and log odds assumption was requisite to develop the logistic model. When this assumption was not met, quantitative variables were categorized based on threshold clinical relevance or based on previous reports (eg, hemoglobin decrease, >2 g/dL). The logistic model aimed to predict the presence of active bleeding was validated internally by a bootstrapping resampling validation method with 200 bootstrap re-samples. The performance of the logistic model in the original data set represents test performance, whereas the performance in the bootstrap sample represents estimation of the apparent performance. The difference between these parameters was averaged to estimate the optimism. The optimism was subtracted from the apparent performance to assess the internally validated performance.[3] All logistic models in our study were created with these principles. Missing values are included in Tables, and no imputation methods were required for the logistic models.

The nomogram for active bleeding was plotted using the nomolog user-command in Stata/IC 14.2 based on the coefficients of the logistic model. This implementation produces nomograms in the way they were conceived by Kattan et al,[4] and subsequently applied in most of the literature without CIs. We assigned points based on the coefficients of the logistic model. Variable scores were rescaled to a range of 0 to 10 to make calculations easier, as follows: anticoagulation: coefficient $\beta 1$: 0.95 → 10 points; electrocautery: coefficient $\beta 2$: 0.95 → 10 points; left-colon location: coefficient $\beta 3$: 0.66 → 7 points; and pedunculated morphology: coefficient $\beta 4$: 0.56 → 6 points.

We decided not to elaborate further (ie, bootstrapping and calibration plots) on the remaining predictive logistic regression: intervention vs no intervention, rebleeding, visible vessel-adherent clot, and moderate-severe bleeding. The reason is that these outcomes may not be as objective as the presence of active bleeding. These analyses should be considered exploratory. The aim of these analyses was to identify those variables with the most substantial influence on bleeding outcomes rather than to quantify the magnitude (OR) of that effect precisely.

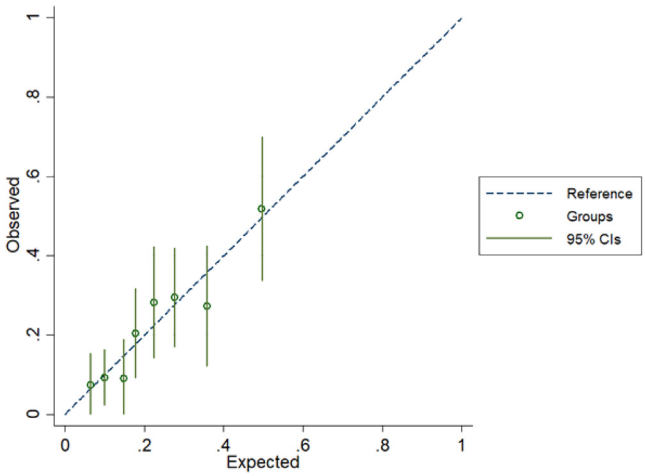
Finally, the variable of no endoscopic, angiographic, or surgical hemostatic intervention was not entered in the final logistic regression model detailed in Table 4 to avoid multicollinearity with the variable of management. Statistical analysis was performed using STATA 14.2.

American Society for Gastrointestinal Endoscopy classification for grading endoscopic adverse events

According to the American Society for Gastrointestinal Endoscopy classification, a mild event included any post-procedural medical consultation, unplanned admission, or prolongation of hospital stay for 3 nights or fewer. A moderate adverse event included any of the following: unplanned anesthesia or ventilation support, hospital stay for 4 to 10 nights, intensive care unit stay for 1 night, transfusion, interventional radiology, or repeat endoscopy. A severe event included unplanned admission for more than 10 nights, intensive care unit stay of more than 1 night, surgery, or a permanent disability.

Supplementary References

1. Domenech JM, Navarro JB. Find the best subset for Linear, Logistic and Cox Regression: User-written command allsets for Stata (computer program). V1.2.4.Barcelona: Graunt 21; 2018.
2. Augustin S, Altamirano J, Gonzalez A, et al. Am J Gastroenterol 2011;106:1781–1795.
3. Steyerberg EW, Harrell Jr FE, Borsboom GJ, et al. Internal validation of predictive models:efficiency of some procedures for logistic regression analysis. J Clinical Epidemiology 2001; 54:774–781.
4. Kattan MW, Eastham JA, Stapleton AM. A preoperative nomogram for disease recurrence following radical prostatectomy for prostate cancer. J Natl Cancer Inst 1998; 90:766–771.



Supplementary Figure 1. Calibration plot of the logistic model intended to predict active bleeding during colonoscopy plotting predicted against observed risk.

Supplementary Table 1. Best Five Models to Predict the Risk of Active Bleeding During Colonoscopy

Variables	Area under the curve	Hosmer–Lemeshow *P* value
1. Anticoagulants, electrocautery, left-sided location, pedunculated morphology	0.73	.73
2. Anticoagulants, electrocautery, left-sided location, pedunculated morphology, hemoglobin decrease >2 g/dL	0.73	.57
3. Anticoagulants, electrocautery, left-sided location, pedunculated morphology, hemoglobin decrease >2 g/dL, comorbidity, ASA ≥III	0.72	.47
4. Anticoagulants, electrocautery, left-sided location, hemoglobin decrease >2 g/dL	0.70	.84
5. Anticoagulants, electrocautery, pedunculated morphology, hemoglobin decrease >2 g/dL	0.70	.70

ASA, American Society of Anesthesiologist.

Supplementary Table 2. Predictors of Moderate–Severe Delayed Postpolypectomy Bleeding

	Mild bleeding N = 127	Moderate–severe bleeding N = 421	Univariate *P* value	Multivariate OR (95% CI); *P* value AUC final model, .70 Hosmer–Lemeshow *P* value = .41
Age, *y*	64.8 (1.1)	68.6 (0.6)	**.002**	Excluded from final model
ASA comorbidity ≥ III	14 (11%)	129 (30.6%)	**<.001**	**2.56 (1.34–4.88); *P* = .004**
Antiplatelet therapy	17 (13.4%)	117 (27.8%)	**.001**	**2.22 (1.22–4.02); *P* = .008**
Anticoagulant therapy	26 (20.5%)	134 (31.8%)	**.01**	**1.8 (1.06–3.08); *P* = .03**
Hemoglobin decrease, >2 g/dL	54 (42.5%)	224 (53.2%)	**.04**	Excluded from final model
INR	1.19 (0.6)	1.21 (0.5)	.89	
Platelets, 10^3/mm^3	208 (58)	206 (45)	.77	
Polyp characteristics				
Size			.74	
<10 mm	35 (27.6%)	102 (24.2%)		
10–20 mm	63 (49.6%)	216 (51.3%)		
>20 mm	29 (22.8%)	103 (24.5%)		
Right-sided colon	49 (38.6%)	166 (39.8%)	.95	
Pedunculated morphology	32 (25.2%)	139 (33%)	.10	
Type of polypectomy				
CBF-CSP	39 (30.7%)	90 (21.4%)		
HSP	88 (69.3%)	331 (78.6%)	**.03**	**1.75 (1.02–2.92); *P* = .04**
Intraprocedural bleeding	23 (18.1%)	52 (85.7%)	.10	
Previous prophylactic hemoclips	24 (18.9%)	129 (30.6%)	**.01**	Excluded from final model
Syncope	3 (2.4%)	30 (7.1%)	**.04**	2.96 (0.90–10.2); *P* = .08
Hemodynamic instability	15 (11.8%)	119 (28.3%)	**<.001**	**2.86 (1.57–5.2); *P* = .001**

NOTE. Quantitative variables are expressed as means (SD). Figures in bold indicate significance.
AUC, area under the receiver operating characteristic curve; ASA, American Society of Anesthesiologist; CBF, cold-biopsy forceps; CSP, cold snare polypectomy; HSP, hot snare polypectomy; INR, international normalized ratio, OR, odds ratio.

Supplementary Table 3. Endoscopic Therapy During Colonoscopy

Variable	
Patients in whom the bleeding point was located	344
Colonoscopy therapy	
None	54 (15.7%)
Hemoclips	235 (68.3%)
Sclerotherapy with adrenaline	150 (43.6%)
Injection of sclerosants	57 (16.6%)
Argon plasma coagulation	11 (3.2%)
Hemospray	1 (1.3%)
Thermal probe	4 (1.2%)
Monotherapy	151 (43.9%)
Combined therapy	139 (40.4%)
Sclerotherapy with adrenaline and sclerosants	43 (12.5%)
Sclerotherapy and hemoclips	114 (33.1%)
Sclerotherapy and argon plasma coagulation	8 (2.3%)
Sclerotherapy and Hemospray	1 (1.3%)
Thermal probe and hemoclips	1 (1.3%)

Supplementary Table 4. Number of Patients in Each Predicted Category for active Bleeding (All 4 Risk Factors, 3 Risk Factors, 2 Risk Factors, 1 Risk Factor, and 0 Risk Factors) in the Whole Cohort (n = 548) and in the Subgroup of Patients in Whom the Nomogram Was Developed (n = 344)

	N = 548	N = 344	Predicted risk
0 risk factors	27 (4.9%)	17 (4.9%)	4%
1 risk factor	188 (34.3%)	109 (31.7%)	7%–12%
2 risk factors	160 (29.2%)	104 (30.3%)	16%–22%
3 risk factors	133 (24.3%)	85 (24.8%)	28%–36%
4 risk factors	40 (7.3%)	29 (8.4%)	50%

NOTE. The 4 risk factors for active bleeding during colonoscopy were active use of anticoagulants, pedunculated morphology, prior use of electrocautery, and left-sided colon.

Supplementary Table 5. Sensitivity Analysis

Variable	Multivariate OR (95% CI), *P* value Area under the curve, 0.71 Hosmer–Lemeshow *P* value = .74
Pedunculated morphology	**1.73 (1.02–3.05); *P* = .04**
Anticoagulant therapy	**2.95 (1.72–5.04); *P* ≤ .01**
Left location	**1.99 (1.06–3.75); *P* = .03**
Previous electrocautery current	**2.85 (1.24–6.65); *P* = .01**

NOTE. The logistic model intended to predict active bleeding during colonoscopy in the initial study population (n = 548), imputing that patients treated without intervention did not present with active bleeding. Figures in bold indicate significance.
OR, odds ratio.

Supplementary Table 6. Predictors of Stigmata of Recent Bleeding: Active Bleeding, Visible Vessel, Adherent Clot

	Significant lesion N = 235	Fibrin-hematin N = 109	Univariate *P* value	Multivariate OR (95% CI), *P* value Area under the curve, 0.71 Hosmer–Lemeshow *P* value = .24
Age, *y*	68.6 (12.6)	68 (12.6)	.67	
ASA comorbidity ≥ III	84 (35.7%)	23 (21.1%)	**.006**	1.68 (0.95–2.97); *P* = .072
Antiplatelet therapy	60 (25.5%)	30 (27.5%)	.69	
Anticoagulant therapy	92 (39.1%)	24 (22%)	**.002**	**2.00 (1.14–3.5); *P* = .015**
Hemoglobin decrease, >2 g/dL	105 (44.7%)	43 (39.5%)	.36	
INR	1.23 (0.6)	1.16 (0.3)	.15	
Platelets, 10^3/mm^3	210 (42)	219 (61)	.42	
Polyp characteristics				
Size			.32	
<10 mm	62 (26.4%)	24 (22%)		
10–20 mm	119 (50.6%)	52 (47.7%)		
>20 mm	54 (23%)	33 (30.3%)		
Location				
Left	152 (65.5%)	58 (53.2%)		**1.76 (1.10–2.83); *P* = .020**
Right	80 (34%)	51 (46.7%)	**.03**	Reference
Missing	3 (21.6%)	0		
Morphology				
Flat-sessile	152 (64.7%)	80 (73.4%)		
Pedunculated	81 (34.5%)	29 (26.6%)	.13	
Missing	2 (0.9%)	0		
Previous use of electrocautery				
No (CBF-CSP)	48 (20.4%)	26 (23.8%)		
Yes (HSP)	187 (79.6%)	83 (76.2%)	.47	
Histology			.96	
Tubular	115 (48.9%)	52 (47.7%)		
Adenoma with villous component	68 (28.9%)	34 (31.2%)		
Serrated	18 (7.6%)	8 (7.3%)		
Invasive adenocarcinoma	5 (2.1%)	3 (2.8%)		
Other	7 (3%)	2 (18.3%)		
Nonretrieved	22 (9.4%)	10 (9.2%)		
Dysplasia			.76	
No	19 (8.1%)	8 (7.3%)		
Low grade	148 (63%)	74 (67.9%)		
High grade	40 (17%)	14 (12.8%)		
Invasive	6 (25.5%)	3 (2.8%)		
Nonretrieved	22 (9.4%)	10 (9.2%)		
Intraprocedural bleeding	33 (14%)	12 (11%)	.44	
Previous prophylactic hemoclips	79 (33.6%)	29 (26.6%)	.19	
Syncope	14 (6%)	5 (4.6%)	.61	
Hemodynamic instability	66 (28.1%)	28 (25.7%)	.64	

NOTE. Quantitative variables are expressed as means (SD). Figures in bold indicate significance.
ASA, American Society of Anesthesiologists; CBF, cold-biopsy forceps; CSP, cold snare polypectomy; HSP, hot snare polypectomy; INR, international normalized ratio.