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Management of delayed bleeding after endoscopic mucosal resection of large colorectal polyps: a retrospective multi-center cohort study

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ABSTRACT

Background and study aims Delayed bleeding (DB) is the most frequent major adverse event after endoscopic mucosal resection (EMR) of large non-pedunculated colorectal polyps (LNPCPs). Evidence-based guidelines for management of DB are lacking. We aimed to evaluate the clinical presentation, treatment and outcome of patients with DB and to determine factors associated with hemostatic therapy.

Patients and methods Patients with DB were identified by analyzing all consecutive EMR procedures for LNPCPs (≥ 2 cm) from one academic center (2012–2017) and seven regional hospitals (2015–2017). DB was defined as any postprocedural bleeding necessitating emergency department presentation, hospitalization or reintervention. Outcome of DB was assessed for three clinical scenarios: continued bleeding (CB), spontaneous resolution without recurrent bleeding during 24 hours observation (SR), and recurrent bleeding (RB). Variables associated with hemostatic therapy were analyzed using logistic regression.

Results DB occurred after 42/542 (7.7 %) EMR procedures and re-colonoscopy was performed in 30 patients (72 %). Re-colonoscopy and hemostatic therapy rates were 92 % and 75 % for CB (n = 24), 25 % and 8 % for SR (n = 12), and 83 % and 67 % for RB (n = 6), respectively. Frequent hematochezia (≥ hourly) was the only factor significantly associated with hemostatic therapy (RR 2.23, p = 0.01). Re-bleeding after endoscopic hemostatic therapy occurred in 3/22 (13.6 %) patients.

Conclusion Ongoing or recurrent hematochezia is associated with a high rate of hemostatic therapy, warranting re-colonoscopy in these patients. A conservative approach is justified when bleeding spontaneously settles, and without recurrent hematochezia during 24 hours observation patients can be safely discharged without endoscopic re-examination.

Introduction

Endoscopic mucosal resection (EMR) is the preferred treatment for large (≥ 2 cm) non-pedunculated colorectal polyps (LNPCPs) [1, 2]. EMR is a minimally invasive technique which has proven to be safe, efficacious, and cost-effective [3, 4].

Delayed bleeding (DB) is the most frequent major adverse event (AE), occurring in 3.7 % to 7 % after colorectal EMR [4–8]. Reported clinical and procedural risk factors include proximal colon location, polyp size ≥ 40 mm, use of anticoagulants, no preventive clipping, age > 75 years, ASA score ≥ III, use of an electrosurgical current not controlled by a microprocessor, and intraprocedural bleeding [5–8]. Remarkably, only limited information is available on the detailed clinical course and management of DB. It has been shown that reintervention is indicated in approximately 35 % to 43 % of DBs, which in the majority is performed by re-colonoscopy [6, 7, 9]. However, identification of patients who require an endoscopic hemostatic intervention has not been fully elucidated [5, 7, 10]. As a consequence, there is a need for clinical tools that can assist in deciding whether re-colonoscopy should be pursued or a conservative approach suffices. Until now, only one study has looked into post-EMR DBs in more detail, evaluating the clinical course and management of 62 cases [9].

The aim of our study was to evaluate management of DB for different clinical scenarios and to examine clinical factors associated with the application of hemostatic therapy in a large multicenter cohort of patients with post-EMR DB.

Patients and methods

Study design and population

This was a retrospective analysis of a multicenter cohort of patients who underwent EMR for large (≥ 2 cm) non-pedunculated colorectal polyps (LNPCPs). Patients were extracted from the OPTICAL study, in which LNPCPs of consecutive patients from eight hospitals (seven non-academic and one academic hospital) were prospectively registered between September 2015 and December 2016 [11]. In addition, patients were collected from a prospective registry of consecutive patients who underwent colorectal EMR in the same academic hospital between March 2012 and October 2017. Patients with DB were identified by evaluating patient files up to 1 month after the EMR procedure. DB was defined as: "any bleeding occurring after the completion of the procedure, necessitating emergency department presentation, hospitalization or re-intervention (repeat endoscopy, angiography, or surgery)" [5]. Self-limited bleeding that did not require medical care or managed on an outpatient basis was not deemed clinically significant.

This study was approved by the Medical Research Ethics Committee of University Medical Center Utrecht (reference number 17/517) and was carried out in accordance with the Helsinki Declaration.

Outcomes and data collection

The primary aim was to assess management of all patients with DB, when classified into three clinical scenarios. A secondary aim was to determine clinical factors associated with use of hemostatic therapy. Use of hemostatic therapy was defined as undergoing any intervention at endoscopy, radiography or surgery to manage bleeding. Conservative treatment and undergoing colonoscopy without endoscopic intervention were defined as no hemostatic therapy. Other secondary outcomes were to identify factors associated with active bleeding seen at the post-EMR site, and to determine risk factors for DB.

Medical records and endoscopy reports of all patients were reviewed. Detailed information about clinical course and management of DB were collected. Patients were classified into three different clinical scenarios which were distinguished based on the initial course of DB: 1. continued bleeding (CB), defined as ongoing hematochezia for at most 24 hours after onset, irrespective of frequency; 2. spontaneous resolution (SR), without recurrent bleeding during a 24-hour observation period with either hemodynamic stability or a stable hemoglobin level (not both) as a prerequisite for discharge; or 3. recurrent bleeding (RB), defined as re-occurrence of hematochezia after a period of at least 6 hours without rectal blood loss. These clinical scenarios have been suggested to be clinically relevant in a previously published algorithm and were also thought to be valuable in our own experience [9]. Furthermore, data on time of onset of bleeding, presence of hemodynamic stability, frequency of hematochezia, hemoglobin levels at presentation, fluid resuscitation, transfusion requirements, findings at re-colonoscopy, rate of recurrent DB, and duration of hospitalization were noted. Onset of bleeding was defined as the moment of presentation at the emergency department. In most cases, EMR was followed by 12 to 24 hours of inpatient observation. In case of DB during inpatient observation, days of admission were counted from the day of onset of bleeding. Hemodynamic instability was defined as heart rate ≥ 100 bpm or systolic blood pressure ≤ 100 mmHg. Active bleeding was defined as spurting or oozing hemorrhage witnessed during re-colonoscopy. Endoscopic hemostatic therapy included any modality with the intention to achieve hemostasis or reduce rebleeding, usually by application of clips, adrenaline injection and/or coagulation therapy (bipolar hemostasis catheter or coagulation forceps). Re-bleeding was defined as DB occurring after hemostatic therapy or after discharge. All aspects of management of DB, including initial treatment, indication for re-colonoscopy and (type of) hemostatic therapy, were left to treating physician.

The following data were extracted of all patients, divided into patient characteristics (age, gender, ASA score, comorbidity and use of anticoagulants), polyp characteristics (size, location, Paris classification and histology) and procedural factors (submucosal lifting-sign, use of adrenaline in submucosal injection, macroscopic complete resection, prophylactic clip closure and intraprocedural bleeding, defined as any bleeding occurring during the procedure necessitating direct hemostatic therapy). Prophylactic clip closure was defined as placement of at least one clip (not always leading to complete closure) with

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the intention to reduce the risk of delayed bleeding and/or perforation. Incomplete resection was defined as macroscopic residual polyp tissue after adjunctive treatment.

Description of EMR procedure

All EMR procedures were performed by an experienced endoscopist (>100 EMRs) or a senior therapeutic endoscopy fellow under their direct supervision. EMR was performed using the injection-assisted technique with snare electrocautery, as previously described [12]. Whether the EMR site was prophylactically closed with clips was left to the endoscopist's discretion. Patients were either discharged after four hours postprocedural recovery or were admitted for one-night observation. Regarding the use of antithrombotic therapy, only aspirin was allowed to be continued during the procedure. In case of another or double antiplatelet agents, the non-aspirin drug was replaced by aspirin or ceased 7 days before the procedure (aspirin continued), respectively. Anticoagulant agents were ceased 3 to 5 days before the procedure. Bridging therapy was used in patients with high thrombotic risk, according to local guidelines. In most cases, antiplatelet and anticoagulant agents were recommended one day after the procedure. Synchronous small polyps (<20 mm) or large (≥20 mm) pedunculated polyps were usually resected during the same procedure, albeit the decision was at the discretion of the endoscopist.

Data analysis

Baseline characteristics of all patients and subjects with DB were analyzed using descriptive statistics. If a patient had two or more polyps resected and the bleeding site was unknown, one polyp was selected at random for analysis. Clinical outcome, management, and use of hemostatic therapy were reported for the three different clinical scenarios.

Multivariable logistic regression analysis with backward stepwise selection was performed to identify factors, including patient-, polyp- and clinical characteristics, associated with use of hemostatic therapy in patients with DB. All variables were checked for collinearity using Pearson's test. Factors with a P value for association of ≤0.2 were incorporated in the final multivariable regression analysis. Due to the high rate of events, relative risks were calculated for statistically significant factors.

Similar analysis was performed for active bleeding witnessed during re-colonoscopy. In addition, risk factors for DB were determined using logistic regression analysis in the entire EMR cohort. Factors with $P<0.2$ in the univariable analysis were considered for multivariable analysis. Analysis was performed using IBM SPSS statistical software, version 24. $P<0.05$ were regarded as statistically significant.

Results

A total of 542 LNPCPs were removed during 482 endoscopic procedures conducted in 469 patients. Forty-seven patients had more than one LNPCP removed during the same procedure: two polyps (n = 36), three polyps (n = 9), four polyps (n = 1), five polyps (n = 1). The majority of LNPCPs (57.2 %) were located in the distal colon. Twenty-seven resections (5.0 %) were incom-

plete, of whom five patients underwent surgery. Baseline characteristics of patients and LNPCPs are shown in ▶ Table 1. Synchronous small polyps were resected in 37.1 % (179/482) of the procedures (median number 2 [range 1–19], median size 6 mm [1–19 mm]). Large (≥20 mm) pedunculated polyps were removed during 26 procedures (5.4 %) (median number 1 [1–4]), median size 25 mm [20–60 mm]).

Characteristics of DB and risk factors

DB occurred in 42 patients (8.7 % and 7.7 % based on the number of endoscopic procedures and LNPCPs, respectively) (▶ Table 1), including 10 patients in whom two or more LNPCPs were removed during the same procedure. Multivariable regression analysis showed that both platelet aggregation inhibitors (OR 2.86 (95 % CI 1.3–6.26), $P=0.009$) and anticoagulants (OR 4.72 (95 % CI 2.12–10.53), $P<0.01$) use within 7 days after the procedure, and increasing polyp size (OR 1.19 (95 % CI 1.01–1.41), $P=0.04$) were independent risk factors for DB (**Supplementary Table 1**). A trend towards a higher DB risk was observed for proximal location (OR 1.9 (95 % CI 0.98–3.66), $P=0.057$). Concurrent polypectomy of small or pedunculated polyps was not a risk factor for DB.

The majority of DBs occurred within 72 hours after EMR (n = 25, 59.5 %). Clinical parameters and management at presentation are shown in ▶ Table 2. Frequent hematochezia (≥hourly) was observed in 13 patients (31.0 %) and in only one patient hemodynamic instability could not be restored by fluid resuscitation, requiring intensive care unit admission. Median duration of hospitalization was 2 days (interquartile range 1–3). The majority of patients with DB (n = 19, 45 %) were included from an academic hospital (**Supplementary Table 2**).

Management for different clinical scenarios

The most common clinical scenario of DB was continued bleeding (n = 24, 57.1 %). DB settled spontaneously in the remaining 18 patients (42.9 %), of whom six developed recurrent bleeding, but the majority (n = 12) had persistent hemostasis during 24-hour observation.

The flowchart of all patients with DB categorized into three distinct clinical scenarios is shown in ▶ Fig. 1. Re-colonoscopy was performed in 30 patients (71.4 %) and was most frequently performed in the CB-group (22/24, 92 %), followed by the RB-group (5/6, 83 %) and SR-group (3/12, 25 %). Endoscopic findings during re-colonoscopy are shown in ▶ Table 3. Active bleeding (n = 6) or stigmata of recent bleeding (n = 18) were found in the majority (88.9 %) of patients with CB or RB. Twenty-two of 30 patients received hemostatic therapy during the first re-colonoscopy (▶ Fig. 2). Hemostatic therapy rates were 18/24 (75 %) in the CB-group and 4/6 (67 %) in the RB-group. In the SR-group, only one of the 12 patients (8 %) underwent hemostatic therapy, this was at a second re-colonoscopy due to a late recurrent bleeding. The clinical outcome of the remaining 11 patients was favorable without readmission or recurrent bleeding.

Endoscopic hemostatic therapy included only clips (n = 14), only coagulation (n = 2), adrenaline and coagulation (n = 2), adrenaline and clips (n = 2), coagulation and clips (n = 1) and

▶ **Table 1** Baseline characteristics of all LNPCPs and subjects with DB.

	All LNPCPs n = 542	DB n = 42
Patient characteristics		
▪ Age, years, mean (range)	68.3 (38–90)	69.4 (58–87)
Gender, n (%)		
▪ Male	330 (60.9)	31 (73.8)
▪ Female	212 (39.1)	11 (26.2)
ASA grade, n (%)		
▪ 1	185 (34.1)	5 (11.9)
▪ 2	261 (48.2)	25 (59.5)
▪ 3 or 4	96 (17.7)	12 (28.5)
Comorbidity conditions[1], n (%)		
▪ None	211 (38.9)	8 (19.0)
▪ Cardiovascular	280 (51.7)	30 (71.4)
▪ Pulmonary	105 (19.4)	11 (26.2)
▪ Renal	43 (7.9)	6 (14.3)
Continued antithrombotic drugs, n (%)		
▪ None	450 (83.0)	30 (71.4)
▪ Platelet aggregation inhibitors[2]	90 (16.6)	12 (28.6)
▪ Anticoagulation[3]	2 (0.4)	–
Use of antithrombotic drugs within seven days after the procedure, n (%)		
▪ None	372 (68.6)	17 (40.5)
▪ Platelet aggregation inhibitors[2]	99 (18.3)	12 (29.5)
▪ Anticoagulation[3]	71 (13.1)	13 (31.0)
Polyp characteristics		
▪ Lesion size, cm, mean (SD)	3.6 (1.7)	4.1 (1.8)
Lesion location, n (%)		
▪ Rectum	67 (12.4)	5 (11.9)
▪ Rectum < 2 cm dentate line	25 (4.6)	6 (14.3)
▪ Rectosigmoid	12 (2.2)	–
▪ Sigmoid	52 (9.6)	2 (4.5)
▪ Descending colon	21 (3.9)	–
▪ Splenic flexure	14 (2.6)	–
▪ Transverse colon	58 (10.7)	4 (9.5)
▪ Hepatic flexure	61 (11.3)	2 (4.8)
▪ Ascending colon	110 (20.3)	8 (19.0)
▪ Cecum	78 (14.4)	10 (23.8)
▪ Cecum appendix involved	11 (2.0)	–

▶ **Table 1** (Continuation)

	All LNPCPs n = 542	DB n = 42
▪ Cecum ileocecal valve involved	33 (6.1)	5 (11.9)
▪ Distal location[4]	310 (57.2)	19 (45.2)
▪ Proximal location[5]	232 (42.8)	23 (54.8)
Paris classification, n (%)		
▪ Is	184 (33.9)	5 (11.9)
▪ IIa	201 (37.1)	21 (50.0)
▪ IIb	7 (1.3)	1 (2.4)
▪ IIc	–	–
▪ III	–	–
▪ IIa + IIc	13 (2.4)	–
▪ IIa + Is	61 (11.3)	7 (16.7)
▪ Isp	10 (1.8)	1 (2.4)
▪ Unknown	66 (12.2)	7 (16.7)
Status of EMR, n (%)		
▪ First EMR	505 (93.2)	37 (88.1)
▪ Residual/recurrence	37 (6.8)	5 (11.9)
Resection, n (%)		
▪ Piecemeal	494 (91.1)	40 (95.2)
▪ En bloc	45 (8.3)	2 (4.8)
▪ Unknown	3 (0.6)	–
Success of resection, n (%)		
▪ Complete	515 (95.0)	40 (95.2)
▪ Incomplete	27 (5.0)	2 (4.8)
▪ Prophylactic clip closure, n (%)		
▪ Yes	463 (85.4)	39 (92.9)
▪ No	79 (14.6)	3 (7.1)
Histology		
Polyp histology, n (%)		
▪ Tubular adenoma	135 (24.9)	11 (26.2)
▪ Tubulovillous adenoma	257 (47.4)	24 (57.1)
▪ Villous adenoma	64 (11.8)	2 (4.8)
▪ Serrated adenoma	55 (10.1)	3 (7.1)
▪ Submucosal invasive cancer	27 (5.0)	2 (4.8)
▪ Lipoma	1 (0.2)	–
▪ Not available	3 (0.6)	–
Dysplasia/cancer, n (%)		
▪ Low-grade dysplasia	395 (72.9)	32 (76.2)

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▶ **Table 2** (Continuation)

	All LNPCPs n = 542	DB n = 42
▪ Low-grade, focal high-grade dysplasia	34 (6.3)	2 (4.8)
▪ High-grade dysplasia	58 (10.7)	6 (14.3)
▪ Submucosal invasive cancer	27 (5.0)	2 (4.8)
▪ None	25 (4.6)	–
▪ Not available	3 (0.6)	–

¹ Sum of percentages is greater than 100 because some patients had several comorbidities
² Including aspirin, clopidogrel, dipyramidole or a combination of these drugs
³ Including acenocoumarol, fenprocoumon, New Oral Anticoagulants or heparin
⁴ Including rectum, sigmoid, descending colon, splenic flexure, transverse colon and hepatic flexure
⁵ Including cecum and ascending colon

▶ **Table 2** Clinical parameters and management at presentation of patients with delayed bleeding.

	DB n = 42
Onset of bleeding, n (%)	
▪ < 24 hours	20 (47.6)
▪ 24–72 hours	5 (11.9)
▪ 72 hours-7 days	10 (23.8)
▪ 8–14 days	7 (16.7)
Clinical course after presentation, n (%)	
▪ Hospital admission	40 (95.2)
▪ Discharge	2 (4.8)
Frequency of hematochezia, n (%)	
▪ < hourly	29 (69.0)
▪ ≥ hourly	13 (31.0)
Hemodynamic stability, n (%)	
▪ Stable	31 (73.8)
▪ Unstable	11 (26.2)
Successful resuscitation with intravenous fluids, n	
▪ Yes	10
▪ No	1
Blood transfusion, n (%)	
▪ No	32 (76.2)
▪ Yes	10 (23.8)

adrenaline, coagulation and clips (n = 1). The rate of rebleeding after endoscopic hemostatic therapy for DB was low, occurring in only three patients (13.6 %). Median duration of hospitalization of the SR-, RB- and CB-group was 1.5, 3.0 and 2.5 days, respectively.

Factors associated with use of hemostatic therapy

Hemostatic therapy was applied in 22 patients (52.4 %) during the first re-colonoscopy. At regression analysis, only frequent hematochezia (≥ hourly) was associated with use of hemostatic therapy (relative risk 2.23, $P = 0.011$) (▶ **Table 4**). No significant associations were found for other patient, polyp, and clinical characteristics, including hemodynamic instability and hemoglobin level. Need of transfusion and ASA score were excluded from analysis due to significant collinearity with hemoglobin level and resumption of antithrombotic drugs, respectively. Also, no no significant differences were found between the groups with (n = 6) and without active bleeding (n = 24).

Discussion

DB is the most common major AE after EMR of LNPCPs, frequently leading to hospitalization and repeated endoscopic examinations. The results of our study show that re-colonoscopy should be strongly considered in patients with CB or RB, particularly in case of frequent hematochezia (hourly or more) as this increases the likelihood of performing hemostatic therapy. On the other hand, re-colonoscopy can be safely omitted when bleeding spontaneously settles because only 8 % received hemostatic therapy during follow-up.

It is still difficult to identify patients with DB who require re-colonoscopy. Because the source of bleeding in post-EMR DB is already known, re-colonoscopy is only required to secure hemostasis or prevent re-bleeding. To our knowledge, this is only the second study providing detailed information on a large cohort of post-EMR 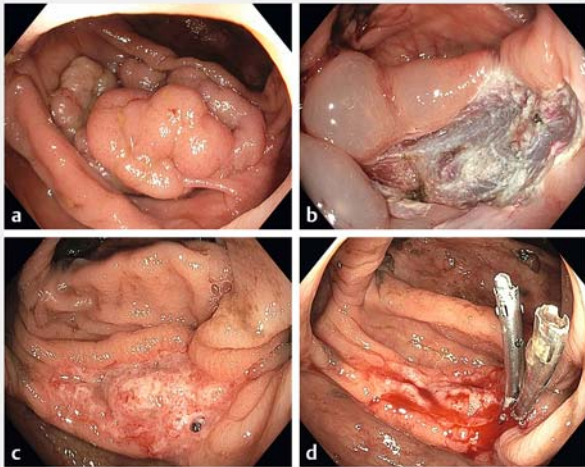DBs. A previous study developed a risk strati-fication by assessing the detailed clinical course and management of 62 DBs after wide-field colorectal EMR [9]. Also, a management algorithm is proposed based on their findings and consensus expert clinical opinion, and emphasizes the importance of ongoing or recurrent hematochezia as incentive for performing re-colonoscopy. In our study we were able to distinguish three different clinical scenarios based on the persistence of hematochezia after onset of bleeding. The highest rate of hemostatic therapy was seen in patients with CB and RB (75 % and 66.7 %, respectively). The majority of re-colonoscopies performed in these patients revealed post-EMR ulcer findings with anticipated high risk of persistent bleeding or rebleeding, including 22 % with witnessed active bleeding and 59 % with a visible vessel or adherent clot. Although evidence-based recommendations are lacking, it is reasonable to believe that, as with gastrointestinal ulcer bleeding, an advantage of hemostatic therapy can be expected in the presence of these high-risk features. The importance of monitoring rectal blood loss is also emphasized by our finding that hematochezia occurring more than hourly was the only clinical parameter associated with hemostatic therapy. In contrast to the previous study, no association was found for blood transfusion [9]. Our cohort in-
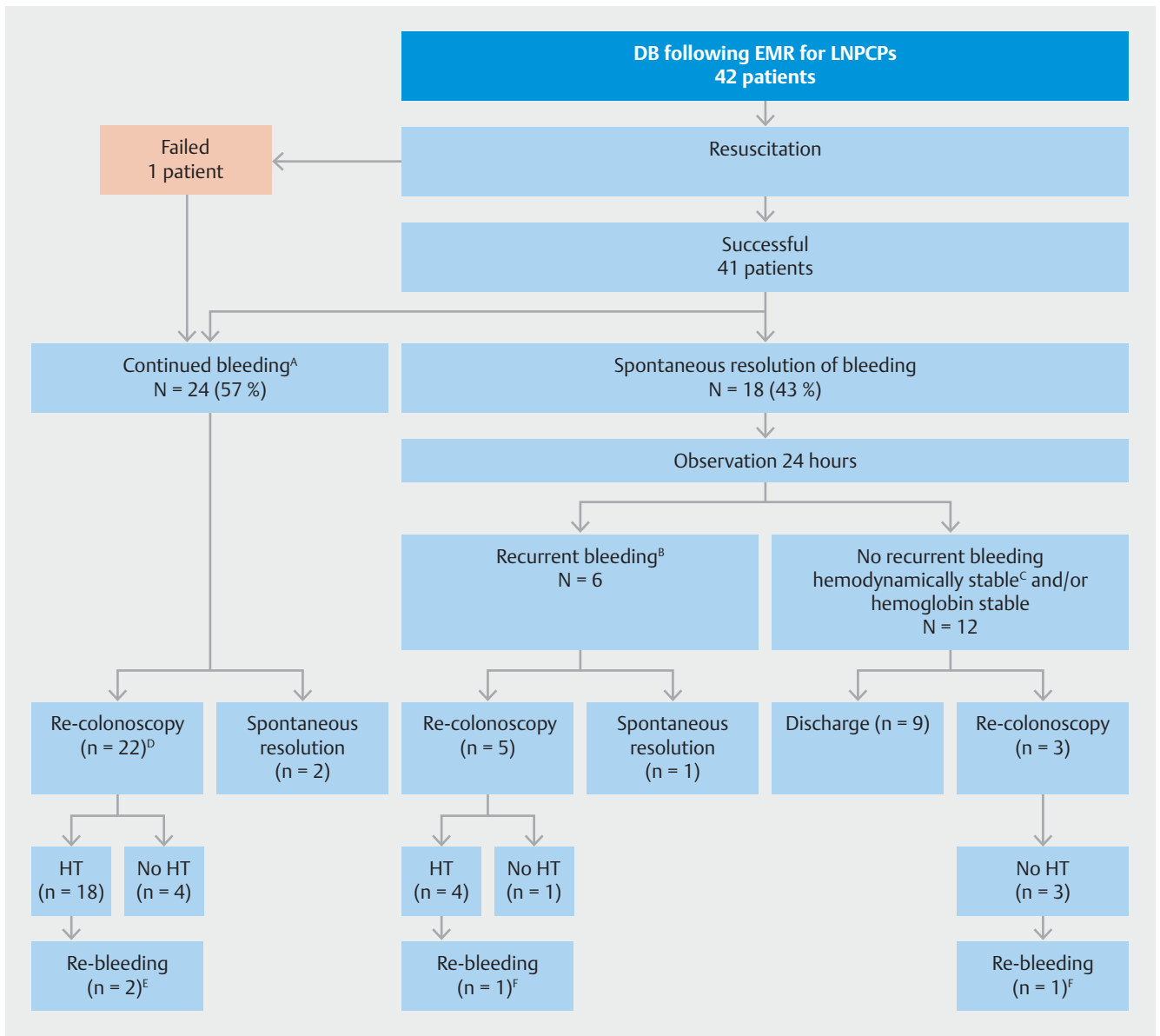
▶ Fig. 1 Management of 42 patients with DB after EMR for LNPCPs for different clinical scenarios. LNPCP, large non-pedunculated colorectal polyp; HT, hemostatic therapy. **A** Ongoing hematochezia for at most 24 hours after onset, irrespective of frequency. **B** Recurrence of hematochezia after a period of at least 6 hours without rectal blood loss. **C** Heart rate < 100 bpm or systolic blood pressure > 100 mmHg. **D** Re-colonoscopy performed ≤ 24 hours, except in one patient who underwent re-colonoscopy 8 days after onset of bleeding. **E** One patient underwent radiographic embolization and one patient was treated conservatively. **F** Hemostatic therapy during second re-colonoscopy.

cluded patients with more severe comorbidity (ASA score ≥ 2 88 % vs. 54 %), elevating the threshold hemoglobin value for blood transfusion [13, 14]. Surprisingly, hemodynamic instability did not increase the application of hemostatic therapy. Because almost all patients presenting with hemodynamic instability were successfully resuscitated, it is likely that a severe, large-volume bleed has discontinued or significantly diminished, reducing the need for hemostatic intervention. Therefore, we believe that re-colonoscopy should be restricted to patients with frequent ongoing or recurrent hematochezia, because they will likely benefit most from performing hemostatic intervention if considered appropriate.

Clinical tools to determine which patients do not require hemostatic intervention are helpful in preventing unnecessary re-colonoscopies and shortening hospital stay. Previous studies suggest that approximately half of DBs after EMR of large colorectal polyps (≥ 2 cm) are self-limiting. Re-colonoscopies rates for DB range between 38 % and 75 % [6, 7, 9, 15, 16], however, data on patients actually receiving hemostatic intervention are limited. Only two studies described management in more detail [9, 16], respectively 50 % and 61 % of patients did not undergo any type of hemostatic intervention, which is in line with our findings. Our results indicate that spontaneous discontinuation of hematochezia appears to be the most relevant clinical

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▶**Fig. 2 a** A 30-mm granular Paris 0-IIa + Is polyp, Hiroshima B, in the ascending colon. **b** Completely resected by piecemeal EMR, some prominent submucosal vessels are seen after resection. **c** DB occurred after 8 days with continued bleeding necessitating re-colonoscopy. A visible vessel was seen, without active bleeding. **d** Hemostatic therapy was used with two hemoclips.

parameter for an indolent course. The majority will not develop recurrent bleeding, even in the long term. It would be of additional benefit to distinguish patients with a high risk of recurrent bleeding, but such a clinical prediction model has not yet been developed for post-EMR DBs. Unfortunately, our study lacks sufficient power to allow solid risk stratification. Recently, the Oakland scoring system has been developed for patients with acute lower gastrointestinal bleeding, incorporating several patient characteristics and clinical parameters at presentation [17]. This model is useful to discriminate patients who can

be safely discharged and is able to predict recurrent bleeding. However, performance was demonstrated in an unselected population with post-polypectomy bleedings accounting for only 2 % of the included patients, which calls into question its applicability in post-EMR DBs. In our DB cohort patients with a low risk score (up to 8), which has been associated with a safe discharge, were absent, and another threshold could not be identified (**Supplementary Table 3**). Although further testing of this model is required in a larger cohort of post-EMR DB, our results suggest that the impact in clinical practice for this specific category of lower gastrointestinal bleeding is probably limited. Therefore, for now, we would advocate a wait-and-see approach if hematochezia resolves spontaneously. It seems safe to discharge these patients after a 24-hour observation period.

One of our secondary outcomes was to identify risk factors for DB. The association of increasing polyp size and antithrombotic drug therapy with DB is consistent with previous studies [6–8, 18]. In the majority of studies also proximal location is marked as a significant risk factor for DB [5–8]. Remarkably, we were not able to detect a significant association, however, a trend was observed when excluding the transverse colon and hepatic flexure from proximal location. Importantly, we believe our results are valid because risk estimates have been adjusted for potential confounders such as prophylactic clip closure.

Several limitations of our study should be mentioned. The main limitation is the small number of DB events, which undermines the validity of our study results. As a consequence, only (strongly) associated factors could be identified rather than the measure of association. Second, we used application of hemostatic therapy as one of our major outcomes, although it remains unclear whether this was truly indicated in our patients. As already mentioned, a validated risk score to estimate re-bleeding risk based on endoscopically assessed post-EMR ulcer bleeding stigmata is lacking. Consequently, it is still unclear which ulcers will benefit from hemostatic therapy. However,

▶**Table 3** Endoscopic findings and hemostatic therapy during first re-colonoscopy.

	Total	Clinical scenarios			Hemostatic therapy		
Endoscopic findings	**n (%)**	**CB**	**RB**	**SR**	**HT**	**Untreated**	**% HT**
Active bleeding							
▪ Spurting hemorrhage	4 (13.3)	4	0	0	4	–	100
▪ Oozing hemorrhage	2 (6.7)	1	1	0	2	–	100
Stigmata of recent bleeding							
▪ Visible vessel	8 (26.7)	6	1	1	7	1	87.5
▪ Adherent clot	10 (33.3)	8	1	1	7	3	70.0
▪ Hematin on ulcer base	2 (6.7)	1	1	0	2	–	100
No stigmata of recent bleeding							
▪ Clean ulcer base	1 (3.3)	–	0	1	–	1	0
▪ Ulcer not found/ visualization not possible	3 (10.0)	2	1	0	–	3	0
▪ Total	30	22	5	3	22 (73 %)	8 (27 %)	

HT, hemostatic therapy; CB, continued bleeding; RB, recurrent bleeding after spontaneous resolution; SR, spontaneous resolution without recurrent bleeding.

▶ **Table 4** Multivariable regression analysis to identify factors associated with use of hemostatic therapy

	No hemostatic therapy n = 20	Hemostatic therapy n = 22	P value	Relative risk
Patient characteristics				
Mean age, years (range)	69.5 (58–83)	69.3 (61–87)		
Gender, n (%)				
▪ Female	4 (36.4)	7 (63.6)		
▪ Male	16 (51.6)	15 (48.4)		
Use of antithrombotic drugs within seven days after the procedure, n (%)				
▪ None	7 (41.2)	10 (58.8)		
▪ Platelet aggregation inhibitors	7 (58.3)	5 (41.7)		
▪ Anticoagulation	6 (46.2)	7 (53.8)		
Polyp characteristics				
Increasing lesion size[1], per cm, mean (SD)	3.85 (1.79)	4.25 (1.79)		
Lesion location, n (%)				
▪ Distal location[1]	9 (47.4)	10 (52.6)		
▪ Proximal location[2]	11 (47.8)	12 (52.2)		
Procedural characteristics				
Prophylactic clip closure after EMR, n (%)				
▪ Yes	3 (75.0)	1 (25.0)		
▪ No	17 (44.7)	21 (55.3)		
Clinical characteristics				
Frequency of hematochezia, n (%)			0.011	Reference 2.23
▪ <hourly	18 (62.1)	11 (37.9)		
▪ ≥hourly	2 (15.4)	11 (84.6)		
Hemodynamic stability, n (%)				
▪ Stable	15 (48.4)	16 (51.6)		
▪ Unstable	5 (45.5)	6 (54.5)		
Mean hemoglobin level at presentation, g/dL (SD)	12.1 (2.3)	12.0 (2.0)		

[1] Including rectum, sigmoid, descending colon, splenic flexure and transverse colon
[2] Including cecum and ascending colon.

we believe that our data are representative of current clinical practice. If the Forrest classification would be applied to the post-EMR ulcers [19], 83.3 % of the patients (20/24) with high-risk endoscopic stigmata (i.e. Ia, Ib, IIa and IIb) received hemostatic therapy and only two patients underwent endoscopic treatment for low-risk stigmata (i.e. IIc and III). It should be stressed that endoscopic hemostatic technique was not standardized and, although clips were most commonly applied, treatment varied widely. Clear recommendations for optimal endoscopic treatment, therefore, cannot be provided, also due to the low number of rebleeding events after hemostatic treatment. Another limitation is that data used for regression analysis were collected at the moment of presentation at the emergency room or in hospital. Because re-colonoscopy was usually not performed directly after presentation, its findings may not accurately reflect the recorded clinical variables. Finally, our study outcomes should not be generalized to patients suffering from DB after cold snare polypectomy or EMR for small colorectal polyps (<20 mm).

Conclusion

In conclusion, our study demonstrates that in patients with DB after EMR for LNPCPs the persistence and frequency of hematochezia should be the determining factors in deciding whether to perform re-colonoscopy. Endoscopic re-examination should only be pursued in case of continued or recurrent bleeding, especially in the presence of frequent hematochezia (≥hourly),

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as it increases the likelihood of performing hemostatic therapy. If patients have no signs of persistent bleeding after resuscitation, they can be discharged safely after a short observation period without the need for re-colonoscopy.

Competing interests

Leon Moons: Consultancy Boston Scientific, Frank Vleggaar: Consultancy Boston Scientific

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