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Natural history of definitive diverticular hemorrhage based upon stigmata of recent hemorrhage and colonoscopic Doppler blood flow monitoring for risk stratification and definitive hemostasis

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Abstract

BACKGROUND AND AIMS—Few prospective reports describe the short term natural history of colon diverticular hemorrhage based upon stigmata of recent hemorrhage and none include blood flow detection for risk stratification or as a guide to definitive hemostasis. Our purposes are to report the 30 day natural history of definitive diverticular hemorrhage based upon stigmata and to describe Doppler probe blood flow detection and as a guide to definitive hemostasis.

METHODS—Different cohorts of patients with severe diverticular bleeding and stigmata on urgent colonoscopy are reported. For 30 day natural history, patients were treated medically. If severe rebleeding occurred, they had surgical or angiographic treatment. Natural history with major stigmata (active bleeding, visible vessel, or adherent clot) and no stigmata or flat spots after washing away clots are reported. Doppler probe detection of arterial blood flow underneath stigmata before and after hemostasis is also reported in a recent cohort.

RESULTS—For natural history patients with major stigmata treated medically had 65.8% (25/38) rebleeding rates and 44.7% (17/38) had intervention for hemostasis. Patients with spots or clean bases had no rebleeding. Doppler probe detected arterial blood flow in 92% of major stigmata, none after hemostasis and no one rebled.

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CONTRIBUTIONS OF THE AUTHORS:

Dennis Jensen designed the prospective cohort studies, secured the funding, applied for the IRB approvals and secured them. He also prepared the original manuscript, edited the versions with comments from co-authors, and submitted the final manuscript.
All authors contributed to the research by evaluation of clinical patients while GI Hemostasis attendings and entering them into prospective cohort studies of definitive diverticular; reviewing and editing the original manuscript and revised versions of it; and approving the final manuscript.

CONCLUSIONS—1. Patients with major stigmata treated medically had high rates of rebleeding and intervention for hemostasis. 2. Patients with clean diverticula or only flat spots had no rebleeding. 3. High rates of arterial blood flow were detected under major stigmata with Doppler probe but with obliteration by hemostasis no rebleeding occurred.

INTRODUCTION

There are very few prospective studies reported about the short term natural history of colon diverticular hemorrhage based upon stigmata of recent hemorrhage - SRH (1–4). Also, there are no prior reports about blood flow under SRH or as a guide to definitive hemostasis in diverticular hemorrhage as determined by an Doppler endoscopic probe (DEP) or any other colonoscopic methods. In contrast, for peptic ulcer hemorrhage, SRH have been used for many years for risk stratification to predict early rebleeding and also as a guide to endoscopic hemostasis (5–7). Recently, DEP for blood flow detection underneath SRH has been reported to improve risk stratification and to document complete hemostasis of non-variceal upper gastrointestinal (UGI) hemorrhage (8,9).

Diverticulosis is reported to be the most common cause of severe colon hemorrhage in most studies (1–4, 9–12). For decades, the standard management of severe or recurrent diverticular hemorrhage has been surgery (3,4,10,11,13–15). In regional referral or large medical centers that have interventional radiology (IR), patients with ongoing hematochezia and active bleeding have another option, which is emergency angiography before colon surgery is considered for emergency diagnosis and control of bleeding (2–4,16,17).

In the last 3 decades, urgent colonoscopy after colon purge has increased in utilization by some groups for patients presenting with suspected colonic hemorrhage for lesion localization, risk stratification, colonoscopic diagnosis, and hemostasis of focal colon lesions with SRH including diverticulosis (1–4, 9–12). When the colon is cleared of clots and blood, skilled colonoscopists sometimes recognize and effectively treat major SRH of diverticular hemorrhage, which are defined as active bleeding, a non-bleeding visible vessel, or an adherent clot resistant to target water irrigation in a single colonic diverticulum during urgent colonoscopy after cleansing the colon with purge (9, 12).

Based upon findings at urgent colonoscopy after cleansing the colon, we previously reported a classification of patients with known colon diverticulosis who were hospitalized for severe hematochezia (1). Those with “definitive diverticular hemorrhage” had a major SRH on a diverticulum whereas “presumptive diverticular hemorrhage” was reported when non-bleeding diverticula were seen without SRH but were thought to be the cause since no other significant lesions to explain the severe hematochezia were found on colonoscopy, anoscopy, push enteroscopy and capsule endoscopy. “Incidental diverticulosis” was reported when some other GI lesion in the colon, foregut, or small intestine had SRH and was diagnosed as the cause of the hematochezia by further GI evaluation (1–4, 9–12).

Urgent colonoscopy after purge affords an incremental improvement over angiography in diagnostic yield. That is because only active bleeding can be localized and effectively treated with angiography, whereas with colonoscopy there is the potential of identifying and

treating non-bleeding SRH such as adherent clots, visible vessels, or flat spots in colonic diverticula and other focal lesions (1, 9). Also, with colonoscopy, an etiologic diagnosis of the bleeding cause can be made that is usually not possible with angiography (9). Non-bleeding SRH, which cannot be visualized by angiography or technetium red blood cell scanning (RBC scan) are postulated to be common SRH of diverticular hemorrhage because they are very prevalent in non-variceal UGI hemorrhage during emergency endoscopy (3,5–7). Nevertheless, RBC scans and angiography are often the first tests used in many hospitals to localize and diagnose patients with severe hematochezia and suspected diverticular hemorrhage, probably because this has been the standard of care for several decades and what physicians and surgeons were taught to do in their training programs (1–4, 9–15).

Recently there have been increasing numbers of case reports of colonoscopic hemostasis of patients with definitive diverticular hemorrhage (based upon SRH) treated with various techniques and these report high rates of definitive hemostasis (1,2,4,18–23). However, none have included a medically treated control group nor are there any randomized controlled studies or large prospective cohort studies that report 30 day outcomes such as rebleeding and non-endoscopic intervention rates for rebleeding in patients treated medically with definitive diverticular hemorrhage and different SRH.

Our purposes in this study are as follow: (1) For patients with definitive diverticular hemorrhage based upon SRH who received medical treatment to describe the short term natural history (e.g., up to 30 days) of rebleeding and intervention rates for control of recurrent bleeding, (2) to compare the rates of rebleeding and intervention on medical treatment up to 30 days for high and low-risk patients, based on SRH, (3) to describe colonoscopic DEP results for blood flow determination under SRH and also in presumptive diverticular hemorrhage for risk stratification before treatment and as a guide to definitive endoscopic hemostasis of definitive diverticular hemorrhage, and (4) to compare the natural history results of rebleeding and intervention on medical therapy with those treated and for recent case reports where endoscopic hemostasis was used during urgent colonoscopy for treatment of definitive diverticular hemorrhage.

METHODS

Patients included in this report all gave written informed consent for inclusion in prospective cohort studies of diagnosis or endoscopic hemostasis of severe hematochezia by the CURE GI Hemostasis Research Group. These studies were approved by Institutional Review Boards (IRB's) before start of the studies. This is a retrospective analysis of those prospectively collected data. Different cohorts of patients are reported. The first cohort was seen between January 2001 and July 2013 and was 28 patients with severe hematochezia who on urgent colonoscopy had some SRH in a colon diverticulum. They were not treated at colonoscopy for various reasons such as being before hemoclip era (and concern for risk of adverse events of thermal coagulation), technical access issues (such as SRH in base and not able to evert the diverticulum for focal treatment), or severe active bleeding. As with peptic ulcer hemorrhage (5–7), major SRH were defined as active bleeding, a non-bleeding visible vessel (NBVV), or an adherent clot (resistant to target jet irrigation). This contrasted to clots that appeared adherent but could be washed out of the diverticulum with target jet irrigation

or suctioned off to reveal minor SRH (e.g. a flat spot in a diverticulum) or no SRH (e.g. a clean based diverticula), as previously described (1–4,9–12). Refer to Figures 1 A–C and 2 A and B for examples of the major and minor SRH or no diverticular SRH. Refer to figure 3 for a diagram of the vascular anatomy of a colon diverticulum. Findings after target jet irrigation are reported and are particularly relevant to DEP results (included below) and our current recommendations about colonoscopic treatments (24).

All patients received medical therapy that consisted of resuscitation, monitoring, red cell and blood product transfusions to correct hypovolemia and coagulopathies, stopping anti-platelet and anti-coagulant drugs, and medical treatment of co-morbidities and constipation. After that, if severe clinically evident bleeding continued or recurred during the hospitalization (as defined by a health care worker who witnessed recurrent or continued hematochezia with hemodynamic instability, and with a decrease in hemoglobin by 2 or more grams after recent transfusion and resuscitation, and/or more red blood cell transfusions), patients were referred for possible colon surgery or interventional radiology (IR) with angiographic embolization. One recent patient in this rebleeding group who was not a candidate for surgery or IR had repeat colon purge and urgent colonoscopy after rebleeding and colonoscopic hemostasis when a major SRH was seen.

A second cohort of 17 medically treated patients with major SRH of diverticular hemorrhage (e.g. active bleeding, NBVV, or clot) who were treated by our group before December 2000 and previously reported upon were also included for comparison and contrast with cohort 1 (1). They were also part of our initial report on definitive diverticular hemorrhage and received medical therapy after urgent colonoscopy (1).

The third cohort was 46 patients with severe hematochezia and a colonoscopic diagnosis of diverticular hemorrhage. When colon DEP became available to our group for blood flow detection, this cohort was studied between January 2009 and July 2014, before and after colonoscopic hemostasis (28). Twenty four patients had definitive diverticular hemorrhage and their major SRH were studied with DEP before colonoscopic treatment. After standard hemostasis (e.g. hemoclipping in the base multipolar probe coagulation – MPEC with pre-injection of 1:20,000 epinephrine for active bleeding or adherent clots), DEP was repeated. For comparison, 22 other patients in this cohort study who had presumptive diverticular hemorrhage (i.e. no site of bleeding found on push enteroscopy, anoscopy, and capsule endoscopy except colon diverticula without SRH on urgent colonoscopy) also had DEP interrogation of blood vessels that were seen in the base or neck of diverticula but lacked SRH (refer to Figure 2 B). In these presumptive diverticular hemorrhage patients 1 or more diverticula were studied in the areas where there was fresh blood or clots but no SRH.

All cohorts of patients were prospectively studied and had urgent colonoscopy after colon purge, as previously described (1–4). During colonoscopies target jet water irrigation and suctioning were used to clear any residual clots and blood and to distinguish SRH. Patients were followed prospectively by our CURE Hemostasis Research Group. Study forms were used to collect demographic, clinical, laboratory, and endoscopic data. Also, all patients were prospectively evaluated up to 30 days and routine outcomes data were recorded by a research coordinator, including blood product transfusions, rebleeding rates (defined as

recurrence of hematochezia 6 hours or more after index colonoscopy with decrease in hemoglobin by at least 2 grams and more units of red blood cell [U RBC] transfusions in addition to those received at baseline for initial resuscitation), interventional radiology procedures for rebleeding, surgeries, adverse events, and deaths.

All data were de-identified and entered into data files by a data manager. SAS was used for data management and analyses. These data were prospective collected and retrospectively analyzed for this report. For demographics and outcomes that had continuous or ordinal variables, measures were compared using non-parametric methods (Wilcoxon Rank Sum test). Fisher exact tests were used for comparison of binary variables. A p value of less than 0.05 was considered statistically significant.

RESULTS

For the first cohort on the natural history study, 7 low-risk patients (with spots or clean based diverticula after clots were target jet irrigated, suctioned, and washed off during urgent colonoscopy) were compared with 21 high-risk patients (those with major SRH in a diverticulum on urgent colonoscopy). The background, transfusions, and colonoscopic findings are shown in table 1. Patients were similar except there were significantly more females in the low-risk group and more were treated before hospitalization with Clopidogrel and fewer took non-steroidal anti-inflammatory agents (NSAIDs) than the high-risk group. The baseline mean hemoglobin was significantly lower in the high-risk group. There were significant differences in transfusion requirements at baseline (higher in the high-risk group) and in the types of SRH seen at colonoscopy after target jet irrigation of the clots or fresh blood in the diverticula (flat spots or clean diverticula after irrigation and suctioning in the low-risk group and no major SRH).

For the 30-day natural history outcome result, see table 2. There were significant differences in all outcomes including higher rebleeding rates, rates of intervention for control of rebleeding, mean hospital days, and mean number of additional GI tests performed after the index colonoscopy for diagnosis and treatment of rebleeding in the high-risk compared with the low-risk group.

For natural history of rebleeding on medical therapy, the outcome results for rebleeding and subsequent intervention for control of bleeding of the high-risk patients with major SRH of both the prior (second cohort described) and the first new cohort are shown in table 3. These are listed by major SRH for all patients who were treated medically. For the different stigmata of hemorrhage, the rates of rebleeding (and intervention to control rebleeding) varied with the different SRH - active bleeding was the highest at 84.2% rebleeding (and 57.9% intervention), NBVV intermediate was 60% (and 40%), and adherent clot was the lowest at 42.9% (and 28.6%).

For these medically treated patients the mean time to diverticular rebleeding was 35 hours, with a median time of 24 hours. The range was 12 hours (more typical of active bleeding patients) to 48 hours (for visible vessels or clot patients) but to a maximum of 7 days (for 1 clot patient). For both the new and older cohorts, these outcomes were very similar.

For the other recent cohort of diverticular bleeding studied with the DEP for detection of blood flow in diverticula risk stratification and as a guide to complete colonoscopic hemostasis, the detection of arterial bleeding results varied according to definitive or presumptive diverticular hemorrhage and by SRH. Overall, 92% of those with major SRH – definitive diverticular bleeds - (22/24) had superficial (<4 mm deep) arterial flow detected by colonoscopic DEP underneath the SRH and for 2 to 4 mm on either side of the SRH along the artery in the diverticulum (refer to figures 1 and 3). No diverticulum had venous blood flow detected with the Doppler probe. Arterial blood flow detection rates were adherent clot 80% (4/5), visible vessel 93% (13/14), and active bleeding 100% (5/5). Because the location of the artery and SRH have been used as guides to definitive hemostasis (and obliteration of arterial blood flow), no patient in this recent cohort had recurrent diverticular hemorrhage. There were no adverse events of colonoscopic hemostasis. In contrast, none of the patients (0/22) with presumptive diverticular hemorrhage and with vessels that could be visualized in the diverticulum had blood flow detected by DEP (refer to figures 2 A and B).

DISCUSSION

This report has the largest number of patients studied prospectively and treated medically that describes the 30-day natural history of colonic diverticular hemorrhage and one of very few based upon different SRH. The 30-day rebleeding rates of patients with major SRH of diverticular hemorrhage are very high and so are the intervention rates for control of recurrent bleeding. Rebleeding and intervention rates were similar for both natural history cohorts. Furthermore, these rates of early rebleeding are higher than those reported for similar SRH in patients with peptic ulcer bleeding (PUBs) treated medically, with high-dose intravenous proton pump inhibitor drugs - PPIs (3,6,7). For example, rebleeding rates for active bleeding PUB's (if oozing and arterial bleeding are combined) are about 50% (vs. 84.2% for definitive diverticular active bleeding); about 40% for NBVV (vs 60% for diverticular NBVV); and about 30% for adherent clot (vs. 43% for diverticula with adherent clots). In contrast, the 30 day rebleeding rates for minor or no SRH (e.g., flat spots or clean based diverticula after washing away clots) are very low and similar to ulcer hemorrhage with these minor SRH (0% rebleeding for diverticulosis vs. 3%–8% for PUD, respectively).

For definitive diverticular hemorrhage, high rates of rebleeding and intervention correlated well with the high rates of superficial (e.g., < 4 mm deep) arterial blood flow detection with DEP under these major SRH. Because there is no effective medical therapy available for controlling active diverticular hemorrhage or preventing early rebleeding of high-risk SRH such as PPI's for bleeding ulcers, we now recommend endoscopic therapy during the index colonoscopy (9,12). Based upon the DEP localization of arterial blood flow under the SRH and for 2 to 4 mm along the underlying artery and also cognizant of the arterial anatomy of colonic diverticula (figure 3), we now recommend treatment endoscopically on and/or on either side of the SRH to obliterate the underlying artery and prevent rebleeding (9, 12, 24). The positive outcomes with no rebleeding are confirmed in follow-up of the recent patients who were treated with DEP as a guide to definitive hemostasis.

The studies of blood flow and artery localization under SRH with DEP have similar therapeutic implications to colonoscopic hemostasis as the histologic studies of non-bleeding visible vessels in peptic ulcers reported by Swain and Johnston over three decades ago (25–27). These give the endoscopist a target for focal treatment during urgent colonoscopy – on or very close to the SRH where the disruption of the underlying artery and the actual bleeding point are located. When colonoscopic treatment has been applied far away from the SRH in other reports, such as at the neck of the diverticulum when the SRH is in the base, diverticular rebleeding rates are quite high as would be expected from the vascular anatomy (Figure 3), because the artery underneath the SRH in the base of the diverticular is still patent and blood flow continues (9, 28–30).

Although RCTs have not been reported for definitive diverticular hemorrhage with major SRH, there are an increasing number of case series that report low rates of rebleeding and subsequent intervention for rebleeding when endoscopic hemostasis is applied on or next to the SRH. Such reports include application of bipolar or multipolar coagulation (particularly at the neck of the diverticulum) and hemoclipping (safer at the base of the diverticulum than thermal coagulation), with or without pre-injection of dilute epinephrine (9). Rubber band ligation has also been reported (9, 29–30). Hemostasis rates are reported to be high and rebleeding rates low with these hemostasis techniques, particularly when compared to those rates reported herein for the short term natural history of definitive diverticular hemorrhage of patients treated medically. This is also confirmed by our patients who had no rebleeding after Doppler guided hemostasis for obliteration of arterial blood flow.

In contrast, there appears to be is no justification for colonoscopic treatment of diverticula with flat spots or clots that can be irrigated or suctioned off to reveal clean based diverticula or only flat spots, without other underlying major SRH. None of the patients in our study with these findings rebled. The only indication for treating the patient with a flat spot in a diverticulum would be that underlying arterial blood flow was detected by DEP, similar to some patients with PUB's who have been studied and have a higher risk for rebleeding than other PUB patients with flat spots and negative DEP (31).

The reasons why patients with colon diverticulosis develop a focal hemorrhage from a single diverticulum is not known. We and others have reported significant associations with clinical factors such as constipation, low fiber diets, NSAIDS, aspirin or anti-platelet drugs, and anti-coagulants (3, 32). On urgent colonoscopy, we previously reported that about 60% of definitive diverticular bleeds (with SRH) were located at or proximal to the splenic flexure, although more than 70% of the patients with severe hematochezia and colon diverticulosis had them anatomically in the descending colon or distally (1–4, 9, 11). We hypothesize that differences in regional blood flow, colon motility, or diverticular vascular anatomy may contribute to this disparity.

The pathogenesis of focal diverticular bleeding and SRH or the explanation of why a single diverticulum bleeds is also unknown. We have reported an association of SRH (particularly NBVV at the neck of a diverticulum) with fecoliths (33). We postulate that there is focal pressure and ischemia on the underlying arterial arcade at the neck or base of the diverticulum by the fecolith, which causes erosion into the underlying artery and

hemorrhage. Refer to Figure 3. One other interesting finding is that 92% of the major SRH of definitive diverticular hemorrhage had detectable superficial arterial blood flow with the DEP (<4 mm below the surface), whereas 0% of those with presumptive diverticular hemorrhage (where the vessels could be seen in the base or neck but no SRH were found) had positive blood flow detected. This indicates that there may be either increased blood flow below major SRH, a larger artery, closer proximity of the artery to the gut lumen in the diverticulum at the SRH, or possibly an aneurysm or another abnormality of the underlying artery in some patients, as has been previously described for NBVV in peptic ulcers (3, 25–27).

Our conclusions are as follows: (1) when definitive diverticular hemorrhage is diagnosed based upon major SRH at urgent colonoscopy and managed medically without endoscopic hemostasis, the rates of clinically significant rebleeding, RBC transfusions, and intervention for control of further bleeding are very high. (2) Rebleeding rates depend upon the SRH with active bleeding having the highest rate of 84.2%, NBVV intermediate at 60%, and adherent clot 42.9%. These rates are higher than peptic ulcers with similar SRH, probably because there is no effective medical therapy similar to PPIs that can decrease rebleeding rates in colon diverticular hemorrhage. (3) Doppler endoscopic probe monitoring of definitive diverticular bleeding detected arterial blood flow underlying major SRH in 92% of such patients but in none with presumptive diverticular hemorrhage and with normal appearing vessels without SRH visualized. (4) When Doppler probe detected arterial flow under SRH and location of the artery was used as a guide to definitive hemostasis, no patient rebled. (5) In recent case reports of colonoscopic hemostasis of definitive diverticular hemorrhage and those where Doppler probe was used for risk stratification and as a guide to hemostasis, the rebleeding and intervention rates are significantly lower than patients treated medically in this report for similar SRH.

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ACRONYMS USED IN NATURAL HISTORY OF DIVERTICULAR HEMORRHAGE – DOPPLER MONITORING OF BLOOD FLOW PAPER

CURE	Center for Ulcer Research and Education
DDRC	Digestive Diseases Research Center
DEP	Doppler endoscopic probe
GI	Gastrointestinal
Hgb	Hemoglobin
MPEC	Multipolar electrocoagulation
NBVV	Non-bleeding visible vessel

NSAIDS	Non-steroidal anti-inflammatory drugs
PPI	Proton pump inhibitor (drug)
PUB	Peptic ulcer bleed
PUD	Peptic ulcer disease
RBC	Red blood cells
RCT	Randomized controlled trial
SRH	Stigmata of recent hemorrhage
TIC	Diverticular
UGI	Upper gastrointestinal
VA	Veterans Administration
VTI	Vascular Technology Incorporated

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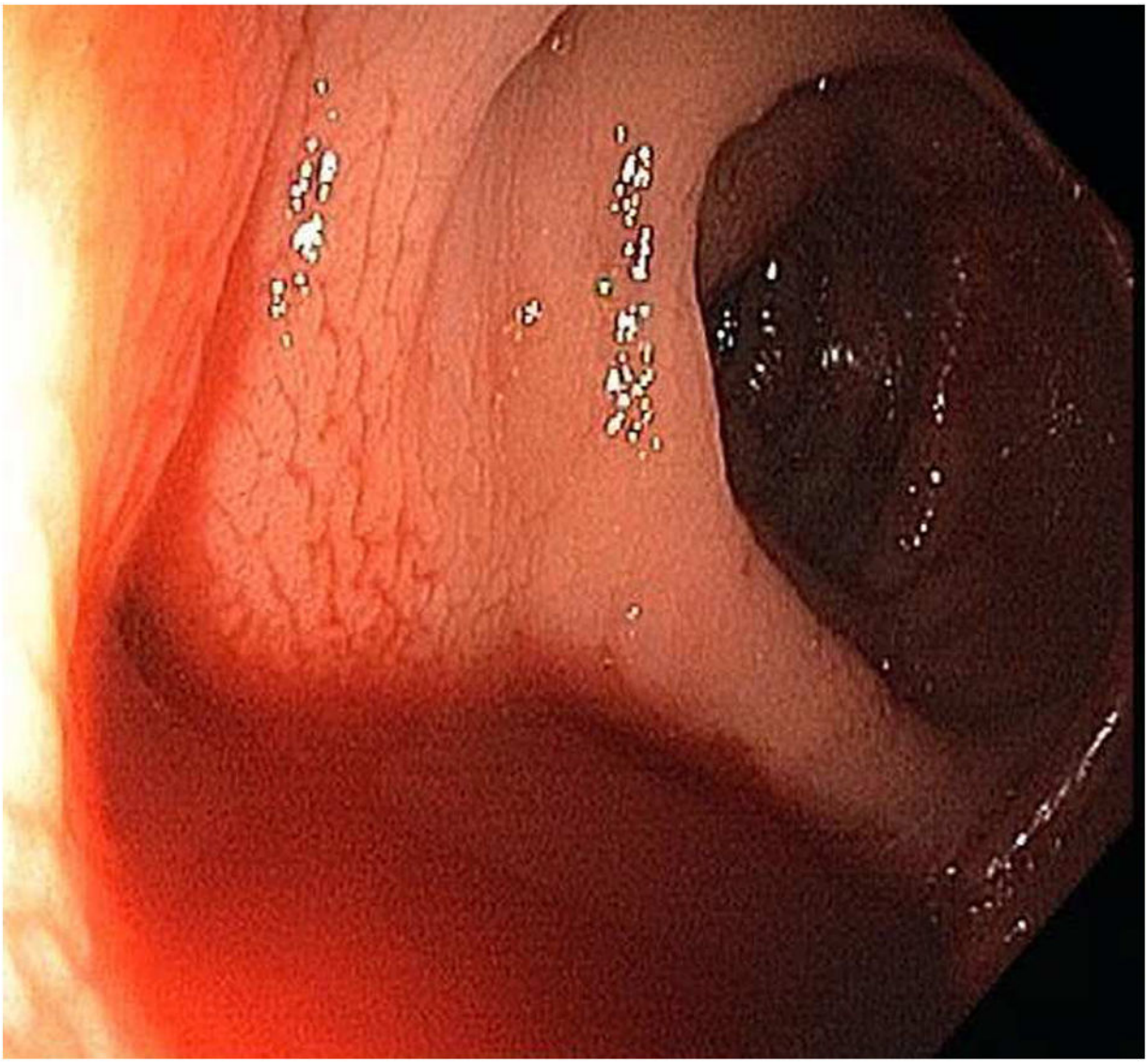

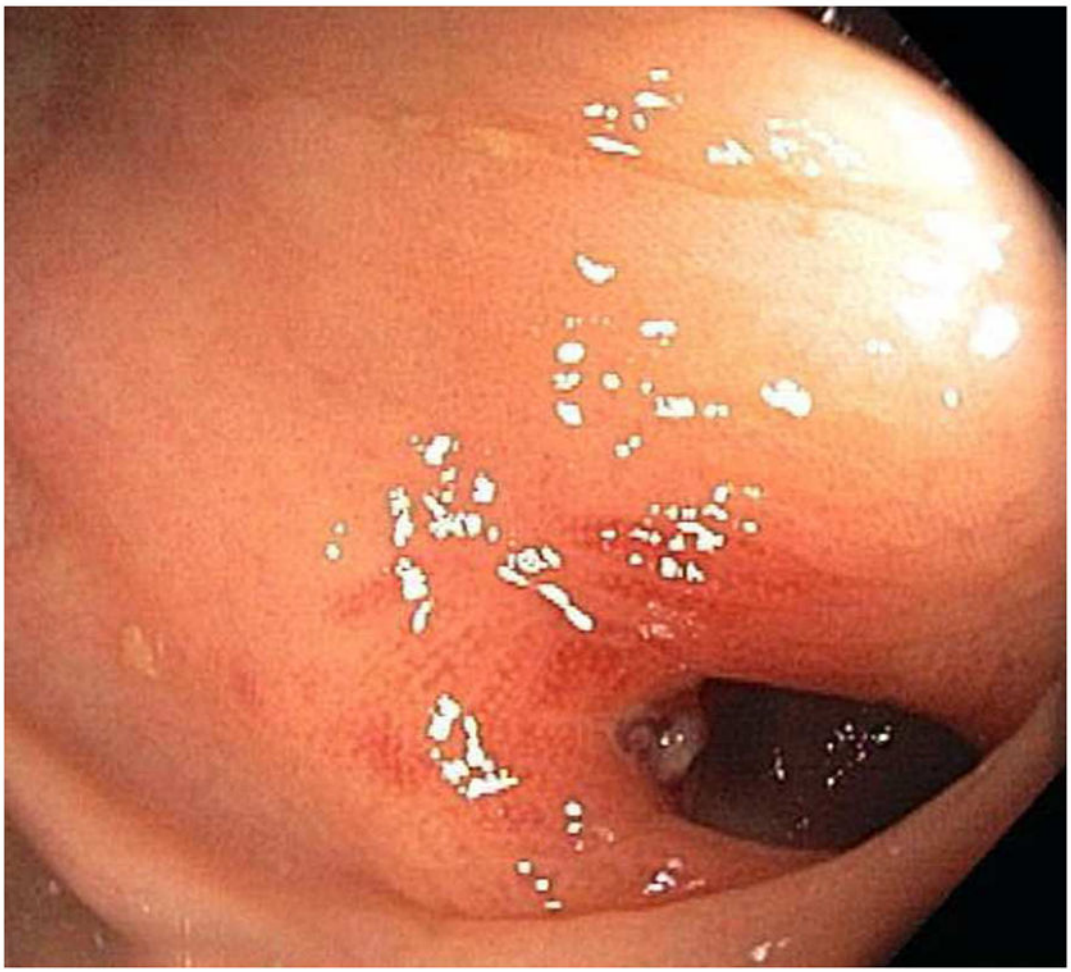

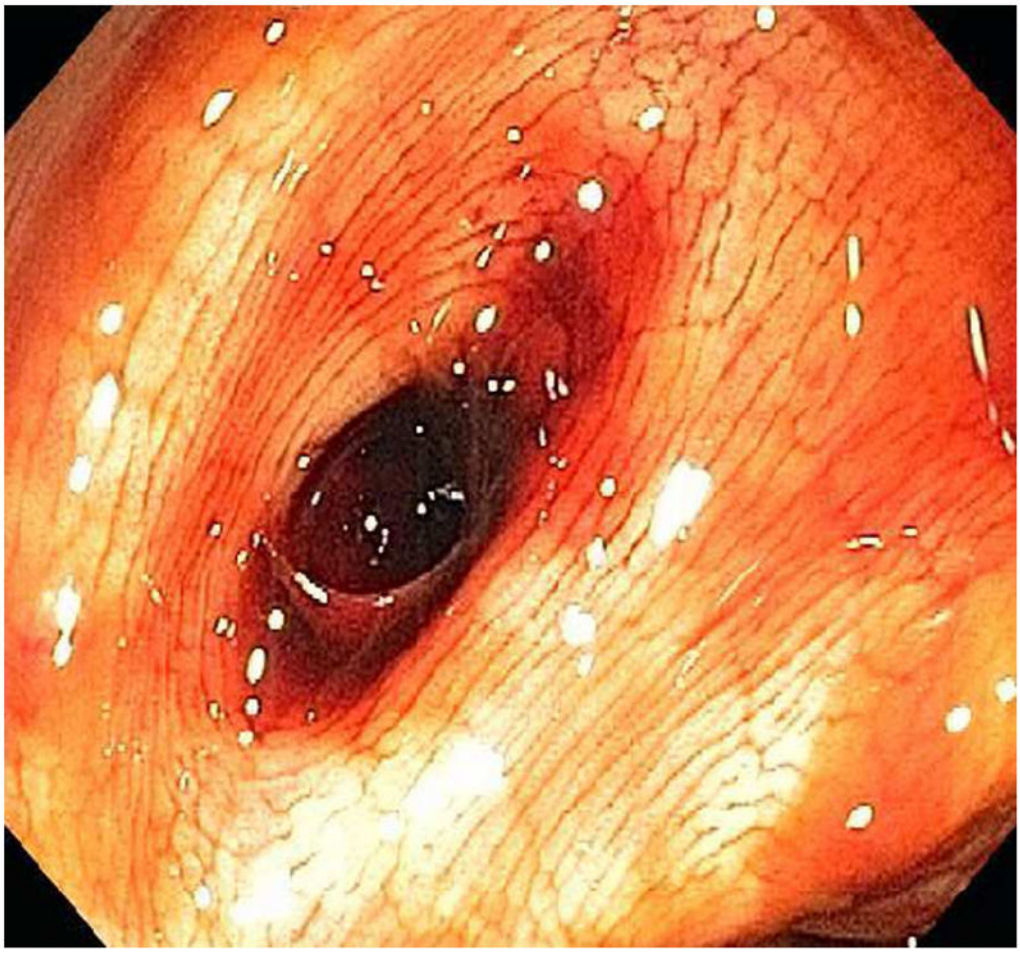

Figure 1.
Major stigmata of colon diverticular hemorrhage – A. Active bleeding, B. Non-bleeding visible vessel. C. Adherent clot.

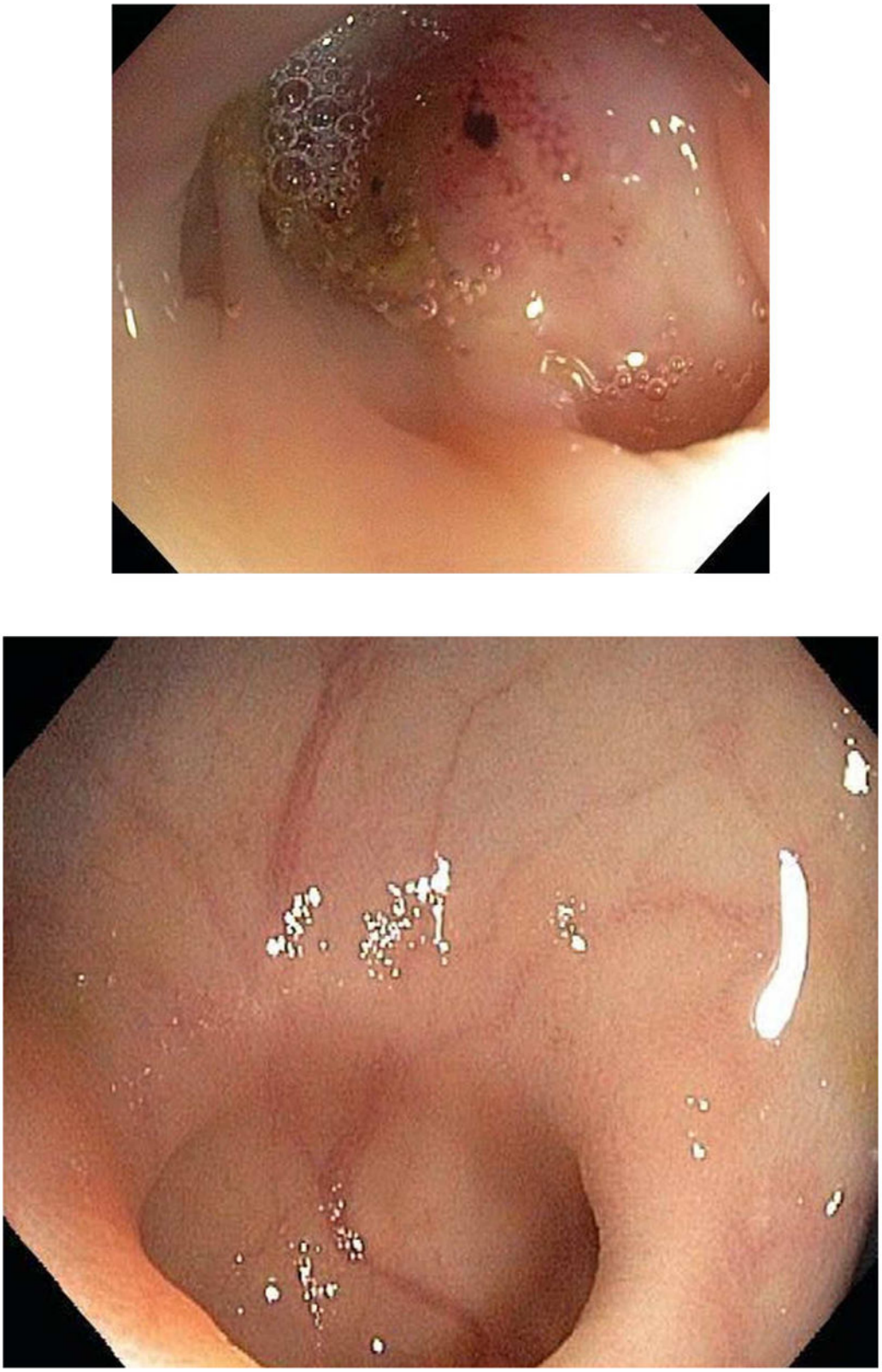

Figure 2.

Minor stigma or no stigmata of recent hemorrhage of colon diverticular hemorrhage. A. Flat spot, B. Clean-based diverticulum with vessels evident.

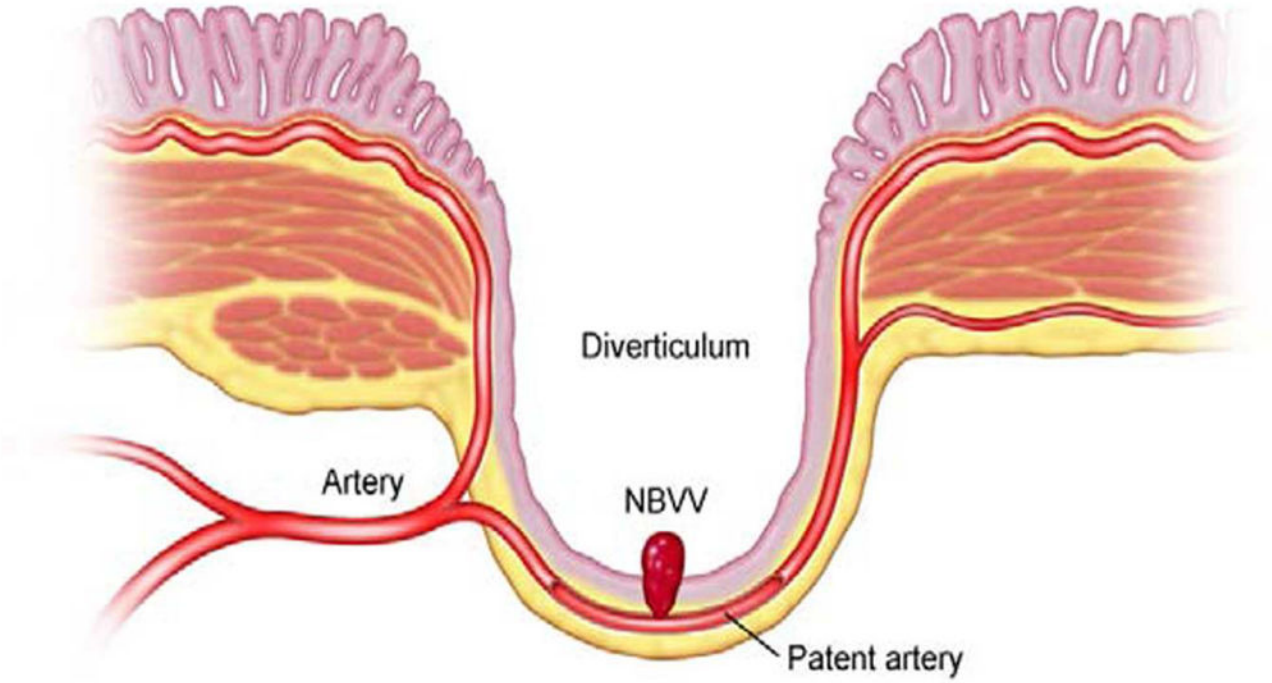

Figure 3.
Diagram of the arterial anatomy of a colon diverticulum with a non-bleeding visible vessel in the base.

Table 1

Baseline characteristics: Low-risk versus high-risk groups by stigmata of hemorrhage – Cohort 1

	Low risk N=7	**High risk N=21**
Age (Mean +/− SD**) (Range)	74 +/− 12 (56–89)	67 +/− 12 (44–84)
Male/Female	2/5*	17/4
Prior Tic Bleeds (Presumptive)	28.5% (2/7)	23.8% (5/21)
Hgb (Mean +/−SD**)	10 +/− 2	9 +/− 1
Recent Bleed Drugs		
Aspirin	42.9% (3/7)	42.9% (9/21)
Clopidogrel	42.9% (3/7)*	0%
NSAIDS	14.3% (1/7)*	52.4% (11/21)
Warfarin	14.3% (1/7)	9.5% (2/21)
Bleed Drugs Before		
0 Bleed drugs	14.3% (1/7)	14.3% (3/21)
1 Bleed drugs	42.9% (3/7)	57.1% (12/21)
2 or More Bleed drugs	42.9% (3/7)	28.6% (6/21)
Mean URBC's to Resuscitate +/− SD** (Range)	2 +/− 1* (0–4)	5 +/− 4 (0–12)
SRH		
Acute Bleed	0*	61.9% (13/21)
NBVV	0*	4.8% (1/21)
Adherent Clot	0*	33.3% (7/21)
Flat Spot	28.5% (2/7)*	0
Clot Removed → No SRH	71.4% (5/7)*	0
Locations in Colon		
Splenic Flexure or Proximal	42.9% (3/7)	47.6% (10/21)
Distal to Splenic Flexure	57.1% (4/7)	52.4% (11/21)
Locations of SRH in TIC		
Neck	28.5% (2/7)	23.4% (5/21)
Base	71.4% (5/7)	76.2% (16/21)

* $p < 0.05$

** SD= Standard deviation

Low-risk group was patients with a fresh clot or red blood that when target jet irrigated revealed a flat spot or clean diverticulum.

High-risk group was patients with active bleeding, non-bleeding visible vessel, or adherent clot after target jet irrigation.

Table 2

Comparison of 30-day Outcomes: low-risk vs. high-risk groups by SRH – Cohort 1

	Low-Risk SRH	High-Risk SRH
Patients	7	21
More Bleeding	0 (0%)	16 (76.2%)*
Interventions for Rebleeding - Totals	0	11 (52.4%)*
Interventional Radiology	0	6 (28.6%)*
Surgery	0	4 (19%)*
Colonoscopic Hemostasis	0	1 (4.8%)
Mean +/− SD** Units RBC for Rebleed	0 +/− 0	4 +/− 4*
Mean +/− SD** Hospital days.	2 +/− 3	9 +/− 6*
Mean +/− SD** Additional major tests	0 +/− 1	2 +/− 2*

* $p < 0.05$

** SD= Standard deviation

For low- and high-risk group descriptions, see table 1.

Table 3

Major Rebleeding and Intervention for Prior and New Cohorts for Major SRH

REBLEEDING & MORE RBC'S	**PRIOR COHORT (#2)**	**NEW COHORT (#1)**	**TOTALS**
Active bleed	4/6	12/13	16/19 (84.2%)
NBVV	2/4	1/1	3/5 (60%)
Clot	3/7	3/7	6/14 (42.9%)
Subtotals	**9/17 (52.9%)**	**16/21 (76.2%)**	**25/38 (65.8%)**
SURGERY, IR, OR COLON TREATMENT			
Active bleed	3/6	8/13	11/19 (57.9%)
NBVV	1/4	1/1	2/5 (40%)
Clot	2/7	2/7	4/14 (28.6%)
Subtotals	**6/17 (35.3%)**	**11/21 (52.4%)**	**17/38 (44.7%)**

NBVV = non-bleeding visible vessel, Clot = adherent clot, IR = interventional radiology, RBC's = red blood cell (transfusions), and SRH = stigmata of recent hemorrhage.