Published in final edited form as:

Dig Dis Sci. 2013 September ; 58(9): 2572–2579. doi:10.1007/s10620-013-2588-y.

LONG-TERM OUTCOMES AFTER SINGLE-BALLOON ENTEROSCOPY IN PATIENTS WITH OBSCURE GASTROINTESTINAL BLEEDING

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Abstract

Background—Limited data exists on the long-term outcomes of patients with obscure gastrointestinal bleeding (OGIB) following single-balloon enteroscopy (SBE).

Aim—To examine the long-term outcomes of patients undergoing SBE for OGIB.

Methods—Consecutive patients undergoing SBE for OGIB at a tertiary care center between 2008 and 2010 were retrospectively identified. Clinical data and SBE findings were extracted from the medical record. Recurrence of OGIB during follow-up through 2012 was assessed by a combination of chart review and telephone interviews.

Results—One hundred and forty-seven patients were included in the study. The overall diagnostic yield of SBE was 64.6% (95/147 patients). Findings of SBE included vascular lesions (VLs, 53.7%), small bowel neoplasm (2.7%), inflammatory lesions (4.8%), and normal SBE (35.4%). One hundred and ten patients [56.4% female, mean age 70.6±11.3 years] were followed for an average 23.9 months after initial SBE. During follow-up, OGIB recurred in 39.5% of patients in whom a source of OGIB was identified on SBE and 55.9% of patients with normal findings on SBE. OGIB recurred in 47.6% of patients in whom small bowel VLs were treated endoscopically. None of the 13 patients in whom a non-VL lesion was identified as the source of bleeding on SBE experienced recurrent bleeding ($p=0.019$).

Conclusions—SBE is a safe and valuable method in managing patients with OGIB. More than 50% of patients experienced no recurrent bleeding during 2 years of follow-up after SBE. The long-term management of OGIB due to small bowel VLs remains challenging.

Keywords

Adult; Gastrointestinal Hemorrhage/therapy*; Gastrointestinal Hemorrhage/diagnosis*; Endoscopy, Gastrointestinal/methods*; Intestine, Small*; Treatment Outcomes; Follow-up Studies

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None of the authors have any financial disclosures related to this manuscript

BACKGROUND

Obscure gastrointestinal bleeding (OGIB), defined as gastrointestinal blood loss for which no etiology can be identified on upper endoscopy, colonoscopy and radiological evaluation, accounts for 5–10% of gastrointestinal bleeding events, and in a majority of cases originates from the small bowel.[1,2] The diagnosis and treatment of OGIB have been revolutionized in the past decade following the introduction of capsule endoscopy and double-balloon enteroscopy (DBE) in 2001. [3,4] In patients with OGIB, DBE has a diagnostic yield of 60–70%, and can deliver endoscopic therapy in a majority of cases where pathology is found. [2,5–10] Several studies have investigated the long-term outcomes of DBE guided therapy for OGIB and found that the long-term remission rate of OGIB after DBE varies from 40–64%. Gerson et al found that bleeding resolved in 59% of patients at 30 months, Shinozaki et al reported 61% of control of bleeding at 29.7 months, and similarly Samaha et al reported the rebleeding rate of small bowel vascular lesions (VLs) was 46% at 36 months.[8,11] It is apparent from previous studies that successful control of OGIB following DBE-guided therapy depends on the underlying etiology; patients with small bowel VLs generally experience higher rates of rebleeding than those with other forms of small bowel pathology. [5,8,11–14]

In 2008, the single-balloon enteroscopy (SBE) system was introduced as an alternative deep enteroscopy technique, with a balloon-tipped overtube sliding over an enteroscope.[15] When compared to DBE, some studies suggest that SBE is less effective in deeply intubating the small bowel and less likely to achieve total enteroscopy (TE).[16,17] On the other hand, a recent randomized multicenter trial demonstrated that SBE achieves comparable insertion depth, TE rate, diagnostic and therapeutic yield when compared to DBE.[6] Regardless of the modality utilized for evaluating the small bowel, in patients with OGIB the key question is whether the procedure results in long-term remission of bleeding, and not the insertion depth, TE rate, or diagnostic yield. While several groups have reported long-term outcomes of patients with OGIB treated with DBE, to date very limited data exists for SBE.[18] The purpose of our study, therefore, was to examine the long-term outcomes of patients undergoing SBE for the evaluation and treatment of OGIB.

METHODS

Patients

Consecutive adult patients (≥ 18 years-old) who underwent SBE at the Barnes–Jewish Hospital/Washington University Medical Center in St. Louis for the evaluation of OGIB between March 2008 and July 2010 were identified from our institutional database for inclusion in the study. Patients were excluded if less than 3 months of follow-up after SBE examination was available, or if SBE was conducted for therapy of bleeding related to hereditary hemorrhagic telangiectasia. This study was approved by the Institutional Review Board of Washington University School of Medicine (# 201102055).

Obscure Gastrointestinal Bleeding

For the purpose of this study, OGIB was defined as gastrointestinal blood loss for which no etiology could be identified on upper endoscopy and colonoscopy.[1] Furthermore, OGIB was sub-classified as: a) overt bleeding from the GI tract as reported by the treating physicians, or 2) occult bleeding, with a ≥ 2 gram/dL drop in hemoglobin from recorded baseline values and positive fecal occult blood with no alternative explanation for anemia. A potential source of OGIB was defined as a lesion in the luminal GI tract with stigmata of recent bleeding (active bleeding, adherent clot, non-bleeding visible vessel, pigmented material at lesion base) in patients with overt bleeding, or luminal GI tract lesions (vascular

malformation, ulcer, polyp, mass, etc) known to cause blood loss in patients with occult bleeding.

SBE Procedure

All SBE procedures were performed by one of 6 experienced endoscopists (CHC, DE, SAE, SJ, DKM, FM), with propofol-based deep sedation administered by a nurse anesthetist under the supervision of an anesthesiologist. SBE procedures were performed using the Olympus SIF Q180 high definition enteroscope and ST-SB1 balloon-tipped overtube (Olympus America, Center Valley, PA). Insertion of the SBE system was accomplished using the “hook-tip” procedure described by Tsujikawa et al.[16] Enteroscopy was initially performed via the oral route in all patients, unless prior endoscopic and radiologic studies indicated that the bleeding source was located in the distal small bowel. When route of examination was determined based on video capsule endoscopy (VCE) findings, the antegrade route was used when pathology was visualized during the initial 75% of small bowel transit time and retrograde SBE was the initial route of examination in the remaining patients.[19] While the depth of insertion was not uniformly recorded, the most distal extent of examination was marked by tattooing with Spot (GI Supply, Camp Hill, PA) in all cases. If the initial examination was non-diagnostic, patients were offered repeat SBE examination via the alternative route in cases where there was evidence of ongoing bleeding and/or a high index of suspicion for a potential source of blood loss in the unexamined portion of the small bowel based on prior studies (VCE or radiographic imaging). Preparation for the SBE procedure consisted of an overnight fast in all patients. Patients who underwent retrograde SBE received standard bowel preparation, consisting of 4 liters of GoLyte[®] on the night prior to the procedure.

Endoscopic therapy was applied when a potential bleeding source or active bleeding was encountered, and the method used was at the discretion of the endoscopists. All ulcers and mass lesions were biopsied and their locations marked by tattooing.

Data Collection

Demographics, results of prior endoscopic procedures, clinical parameters, comorbid medical illnesses and medication lists were recorded from electronic medical records. The overall burden of comorbid conditions was quantified using the Charlson comorbidity index (CCI).[20]

Post- SBE Follow-Up

Follow-up evaluation was performed at an average of 23.9 ± 10.3 months after the SBE, with follow-up data being collected through March 2012. Follow-up information was obtained from our institution’s electronic medical records and/or telephone contact with the patients. A minimum of 4 attempts were made to contact each patient by telephone. At the time of telephone interview, patients who agreed to participate in the study were asked whether they had experienced any recurrent OGIB, defined as recurrent overt bleeding, hospitalization for GI bleeding, further interventions (endoscopic, radiologic, or surgical procedures), or need for blood transfusion or iron therapy. When applicable, cause of death was determined from the medical record.

Statistical analysis

Data are reported as mean $\pm$ standard error for normally distributed data, and median and range for skewed data. Grouped continuous variable data were compared using two-tailed Student’s *t* test and Mann-Whitney U test where appropriate. Intergroup and categorical comparisons were made using the Chi-square and Fisher’s exact tests. A *p* value of <0.05

was required for statistical significance. All statistical analyses were performed using PASW 19.0 (SPSS, Inc., Chicago, IL).

RESULTS

Baseline Demographics

Between March 2008 and July 2010, 147 patients [69.6±12.7 years old, 78 (53.1%) female] underwent SBE for the evaluation of OGIB. Follow-up information was available for 110 patients whereas 37 patients were lost to follow-up (Table 1). There were no significant differences in baseline demographic characteristics between patients who were available for follow-up versus those who were lost to follow-up. Patients who were available for follow-up were more likely to have positive endoscopic findings (69.1% vs. 51.4%, $p=0.011$) and undergo SBE directed therapy (69.1% vs. 35.1%, $p<0.001$) than patients who were lost to follow-up.

SBE Findings and Interventions

A total of 150 SBE procedures were performed during the study period in 147 patients, including 146 SBE via the oral route (antegrade) and 4 via the anal route (retrograde). The average duration of the SBE procedure was 79.4±22.9 minutes. Prior to SBE, patients had undergone a median of 3 [range 1–7] endoscopic procedures, and 103 (70.5%) patients had undergone a video capsule endoscopy (VCE) either with the referring physicians or at our institution. Small bowel pathology was identified on VCE in 94 (91.3%) cases, while the remaining 9 patients had normal findings on VCE. The source of OGIB was identified by SBE in 95 of 147 (64.6%) patients, and includes VLs (angiodectasias and Dieulafoy's lesions) in 79 patients (53.7%), small bowel mass in 4 (2.7%) patients, and inflammatory lesions (ulcers or erosions) of the small bowel in 7 patients (4.8%) (Table 1). Previously missed foregut ulcerations were found in 5 (3.4%) patients (3 Cameron ulcers, 2 duodenal ulcers). SBE was normal to the depth of insertion in 52 patients (35.4%). There was no significant difference in the diagnostic yield of SBE performed in patients with overt OGIB versus occult OGIB (62.5% and 67.1% respectively, $p=0.56$). Endoscopic therapy was performed in 76 (51.7%) patients and eight patients were referred to surgery. The only complication of SBE was a micro-perforation of the distal jejunum related to argon plasma coagulation of a VL, which was successfully managed conservatively.

Recurrent Bleeding in Long-Term Follow-Up

One hundred and ten patients were available for follow-up and 50 (45.1%) of them experienced recurrent OGIB. Recurrent OGIB was not associated with any demographic characteristics, nadir hemoglobin level, comorbid conditions, antiplatelet or anticoagulation therapy, or initial presentation as overt or occult bleeding (Table 2). The diagnostic yield of SBE did not differ significantly between procedures performed at an inpatient (20/31) versus outpatient setting (56/79; $p=0.5$). There was a trend towards increased risks of recurrent bleeding in patients with valvular heart disease and in patients who had SBE performed as outpatients ($p=0.1$ and $p=0.08$ respectively). The pattern of recurrent bleeding changed in 19 of 50 (40.4%) patients. In the 55 patients who initially presented with overt bleeding, 15 (26.8%) patients experienced only occult blood loss during follow-up, while 4 of 55 (7.1%) patients who initially presented with occult bleeding developed overt bleeding during follow-up. Although the pattern of bleeding changed in these patients, the diagnosis did not change during follow-up. Twenty (40%) patients required blood transfusions while the remaining 30 were managed with oral or parenteral iron replacement therapy.

Twenty patients (18%) died during follow-up, at an average of 1.4±0.7 years after SBE. One patient died secondary to abdominal sepsis following small bowel resection, 1 from sepsis in

the setting of massive gastrointestinal bleeding, 5 from cardiovascular diseases, 5 from malignancies, 2 from end stage liver disease, 2 from end stage renal disease, and in 4 patients the causes of death were unknown.

SBE Findings and Recurrent GI Bleeding

The details of SBE findings in patients with follow-up are summarized in Table 3. Recurrent OGIB occurred in 31 of 76 patients (40.8%) in whom SBE revealed a source of OGIB, and in 19 of 34 patients (55.9%) in whom SBE was normal ($p=0.11$). Recurrent bleeding occurred in 47.6% of patients who had VLs identified as the source of OGIB, which was not significantly different from the rebleeding rate of patients who had no pathologic findings on SBE (55.9%, $p=0.47$). On the other hand, if the identified cause of GI bleeding was not VLs, rebleeding occurred in 0 of 13 patients ($p<0.001$).

Therapeutic interventions based on SBE findings were performed in 76 patients. Endoscopic therapy directed at VMs was performed in 63 patients, of whom 31 (49.2%) experienced recurrent bleeding. There was no significant difference in the rates of rebleeding between VLs that were actively bleeding during SBE (6/17, 35%) versus VLs that were not bleeding during SBE (25/46, 54%, $p=0.21$).

Patients who received medical (proton pump inhibitors for peptic ulcers, chemotherapy for lymphoma, biologics for Crohn's disease, octreotide for radiation enteritis) or surgical therapy based on SBE findings were significantly less likely to have a recurrence of OGIB than those who received endoscopic therapy during SBE (0 vs. 49.2%, $p=0.019$). In 3 patients with active bleeding during SBE, primary hemostasis could not be achieved endoscopically. Subsequently, 2 patients with VLs underwent emergent resection of the endoscopically marked small bowel segments and 1 patient with jejunal ulcer secondary to NSIADs was treated with angiographic embolization. None of these patients experienced recurrent OGIB.

During follow-up, 44 of 49 patients with persistent OGIB underwent 89 additional endoscopic and radiologic procedures, averaging 1.6 additional procedures (0–4) per patient. The remaining five patients with persistent occult gastrointestinal blood loss were managed conservatively with iron replacement therapy. Twenty-three patients underwent repeat SBE, with 15 of the procedures being performed for re-treatment of small bowel VLs. Eight patients with negative findings on initial SBE underwent a repeat examination, with negative findings in all cases. Additionally, three patients with recurrent overt bleeding underwent bidirectional DBE during follow-up. The findings of DBE were concordant with those of SBE: 2 patients with VLs, 1 without abnormality. OGIB persisted following DBE in all patients.

An etiology for OGIB was established during follow-up in 5 of 34 patients who had initial normal SBE. Colonoscopy revealed Crohn's disease of the terminal ileum in one patient who subsequently underwent a small bowel resection, and large internal hemorrhoids in another patient who underwent hemorrhoidectomy; in both cases OGIB resolved postoperatively. Angiography identified one small bowel VL, which was successfully treated with coil embolization. Capsule endoscopy detected an ulcerated small bowel carcinoid tumor, which was surgically resected. Computer tomography enterography (CTE) identified a chronically ischemic segment in the mid-ileum of a patient with sclerosing mesenteritis which was surgically resected.

DISCUSSION

In this retrospective cohort study, we reported the long-term outcomes of 110 patients following SBE performed for the evaluation of occult and overt OGIB. The diagnostic yield of SBE was 64.6%, with vascular lesions being the predominant etiology of OGIB, and is in line with the previously reported diagnostic yield of SBE, which has ranged from 35 to 70%, [6,21]. When the etiology of OGIB was identified on SBE, SBE-directed endoscopic, medical, and surgical therapy resulted in a long-term remission of OGIB in 59.2% of patients.

During follow-up, OGIB recurred in 48% of patients with vascular lesions, 56% of patients with normal SBE, and 45% for all patients. The overall rebleeding rate of our patients after SBE was 45% with an average of 23.9 months follow-up. This is similar to the 42% and 39% rebleeding rate reported by Gerson and Shinozaki respectively in OGIB patients at 30 months follow-up after DBE (Table 4). Furthermore, in Gerson's study the rebleeding rate decreased overtime, which may have been due to the definite treatment of lesions found or spontaneous cessation of bleeding. Therefore, it is possible that had we followed our patients longer, the rebleeding rate after SBE may be lower than 45%.

The rebleeding rate of VLs in our study was 48%, which is also similar to the reported rebleeding rate of VLs after DBE (Table 4). Notably, the rate of recurrent bleeding in our patients with VLs was not significantly different from that in those who had an unremarkable evaluation of SBE (48.4% vs. 55.9%, $p=0.47$). The rebleeding rate of patients with normal DBE in Gerson's study was also similar to the rebleeding rate of VLs (45% vs. 42%). This leads us to speculate that in the majority of patients without abnormalities found on deep enteroscopy, the cause of OGIB was due to small bowel VLs not detected by the deep enteroscopy. Indeed, significant small bowel pathology missed by the initial SBE was subsequently identified in only 4 (11.8%) patients in our study, which is similar to the miss rate of 10.9% based on the data from Gerson et al.[8] Recently, Agrawal et al have observed that significant small bowel pathology was identified by CTE in 50% of patients with overt OGIB and non-diagnostic capsule endoscopy.[22] Indeed one patient in our study had significant small bowel pathology discovered by CTE (ischemic small intestinal segment caused by sclerosing mesenteritis). In view of these results, we believe that CTE or MRE should be pursued in patients with persistent overt OGIB and negative endoscopic evaluations.

In a study of the long-term outcome of small bowel VL treated by DBE and argon plasma coagulation, May et al found that patients' overall transfusion requirement declined and the hemoglobin levels increased, yet the rebleeding rate was still 42% at 55 months follow-up. [14] Similarly, we found that despite additional evaluation following SBE, close to half of our patients had persistent OGIB. Small bowel VLs are difficult to treat definitely for multiple reasons. VLs tend to occur in multiple locations and may not be easily detected during endoscopy. Additionally, VLs also tend to recur if the underlying medical conditions predisposing to VL recurrence are not corrected. Moreover, the 40–50% long-term rebleeding rate of VLs in our and other deep enteroscopy studies mirrors the rebleeding rate of VLs in the placebo arms of randomized controlled trials of pharmacologic therapy for small bowel VLs.[23,24] Considering the cost and the potential complications of repeated deep enteroscopies for the treatment of VLs, a comprehensive approach with the combination of endoscopic treatment and medical therapy may be needed to achieve a better and more cost-effective outcome.

In contrast to patients with small bowel VLs or normal SBE, no recurrent OGIB was observed in patients with inflammatory or neoplastic etiologies ($p<0.001$), also consistent

with the findings seen in DBE.[8,11] Therefore, balloon-assisted enteroscopy, whether DBE or SBE, is most effective in identifying small intestinal inflammatory and neoplastic pathologies and in directing subsequent medical and surgical therapy.

In this study, we attempted to identify risk factors for recurrent OGIB following SBE. However, we did not find an association between any patient's clinical or endoscopic factors and the risk of recurrent OGIB. In the subgroup of patients with VLs, we did not find a significant correlation between recurrence of gastrointestinal bleeding and the previously described risk factors for recurrent bleeding (valvular heart disease, number of observed lesions or use of anticoagulation).[5,25] This may be due to the fact that our study population had a high burden of systemic disease (median CCI 2.8), and thus the effect of these risk factors was overshadowed by the unmeasured confounders. It is also possible that our study was underpowered to detect the significant association.

The major limitation of our study is its retrospective nature and limitations inherent to this study design. Loss of patients follow-up is another limitation. We attempted to minimize the impact of these factors by obtaining additional follow-up information through telephone interviews. We also found no significant difference between the patients with or without follow-up. Thirdly, SBE was performed mostly via the oral approach in our practice, and retrograde SBE was only pursued when a high index of suspicion for lesion in the distal small bowel was present based on prior capsule endoscopy or cross-sectional imaging. We do not believe that this significantly limits the generalizability of our results, as prior studies in patients undergoing bidirectional DBE have shown that most lesions responsible for OGIB are located in the proximal small bowel.[8,9,26] A final limitation is that due to the retrospective nature of the study, the insertion depth of SBE was not uniformly recorded and thus not reported in this study. Nevertheless, the main purpose of our study was to investigate the impacts of SBE on the clinical outcome of OGIB, not the insertion depth or TE rate. In addition, the fact that the diagnostic yield and the long-term outcome of SBE presented here are similar to the previously reported literature suggests that the insertion depth of SBE in this study is probably comparable to other studies, and does not affect our results.

In conclusion, SBE is a safe and effective procedure for evaluating and treating patients with OGIB. At an average of 23.9 months follow-up after SBE, 54.5% of patients experienced no further bleeding. The rebleeding rate of patients treated by SBE in this study appears to be similar to the outcome observed in patients undergoing DBE for OGIB. Whereas there was no recurrent bleeding in patients who had inflammatory or neoplastic lesions identified on SBE, close to half of the patients who have small bowel VLs or normal SBE had recurrent OGIB. The optimal management of patients with small bowel VLs remains unclear.

References

1. Zuckerman GR, Prakash C, Askin MP, Lewis BS. AGA technical review on the evaluation and management of occult and obscure gastrointestinal bleeding. *Gastroenterology*. 2000; 118:201–221. [PubMed: 10611170]
2. Raju GS, Gerson L, Das A, Lewis B. American Gastroenterological Association (AGA) Institute technical review on obscure gastrointestinal bleeding. *Gastroenterology*. 2007; 133:1697–1717. [PubMed: 17983812]
3. Yamamoto H, Sekine Y, Sato Y, Higashizawa T, Miyata T, et al. Total enteroscopy with a nonsurgical steerable double-balloon method. *Gastrointest Endosc*. 2001; 53:216–220. [PubMed: 11174299]
4. Iddan G, Meron G, Glukhovskiy A, Swain P. Wireless capsule endoscopy. *Nature*. 2000; 405:417. [PubMed: 10839527]

5. Samaha E, Rahmi G, Landi B, Lorenceau-Savale C, Malamut G, et al. Long-Term Outcome of Patients Treated With Double Balloon Enteroscopy for Small Bowel Vascular Lesions. *Am J Gastroenterol*. 2011
6. Domagk D, Mensink P, Aktas H, Lenz P, Meister T, et al. Single- vs. double-balloon enteroscopy in small-bowel diagnostics: a randomized multicenter trial. *Endoscopy*. 2011; 43:472–476. [PubMed: 21384320]
7. Barreto-Zuniga R, Tellez-Avila FI, Chavez-Tapia NC, Ramirez-Luna MA, Sanchez-Cortes E, et al. Diagnostic yield, therapeutic impact, and complications of double-balloon enteroscopy in patients with small-bowel pathology. *Surg Endosc*. 2008; 22:1223–1226. [PubMed: 17943366]
8. Gerson LB, Batenic MA, Newsom SL, Ross A, Semrad CE. Long-term outcomes after double-balloon enteroscopy for obscure gastrointestinal bleeding. *Clin Gastroenterol Hepatol*. 2009; 7:664–669. [PubMed: 19514115]
9. Sanaka MR, Navaneethan U, Kosuru B, Yerneni H, Lopez R, et al. Antegrade is more effective than retrograde enteroscopy for evaluation and management of suspected small-bowel disease. *Clin Gastroenterol Hepatol*. 2012; 10:910–916. [PubMed: 22610006]
10. Teshima CW, Kuipers EJ, van Zanten SV, Mensink PB. Double balloon enteroscopy and capsule endoscopy for obscure gastrointestinal bleeding: an updated meta-analysis. *J Gastroenterol Hepatol*. 2011; 26:796–801. [PubMed: 21155884]
11. Shinozaki S, Yamamoto H, Yano T, Sunada K, Miyata T, et al. Long-term outcome of patients with obscure gastrointestinal bleeding investigated by double-balloon endoscopy. *Clin Gastroenterol Hepatol*. 2010; 8:151–158. [PubMed: 19879968]
12. Fujita M, Manabe N, Honda K, Tarumi K, Murao T, et al. Long-term outcome after double-balloon endoscopy in patients with obscure gastrointestinal bleeding. *Digestion*. 2010; 82:173–178. [PubMed: 20588030]
13. Kaffes AJ, Siah C, Koo JH. Clinical outcomes after double-balloon enteroscopy in patients with obscure GI bleeding and a positive capsule endoscopy. *Gastrointest Endosc*. 2007; 66:304–309. [PubMed: 17643704]
14. May A, Friesing-Sosnik T, Manner H, Pohl J, Ell C. Long-term outcome after argon plasma coagulation of small-bowel lesions using double-balloon enteroscopy in patients with mid-gastrointestinal bleeding. *Endoscopy*. 2011; 43:759–765. [PubMed: 21544778]
15. Kawamura T, Yasuda K, Tanaka K, Uno K, Ueda M, et al. Clinical evaluation of a newly developed single-balloon enteroscope. *Gastrointest Endosc*. 2008; 68:1112–1116. [PubMed: 18599052]
16. Tsujikawa T, Saitoh Y, Andoh A, Imaeda H, Hata K, et al. Novel single-balloon enteroscopy for diagnosis and treatment of the small intestine: preliminary experiences. *Endoscopy*. 2008; 40:11–15. [PubMed: 18058613]
17. Takano N, Yamada A, Watabe H, Togo G, Yamaji Y, et al. Single-balloon versus double-balloon endoscopy for achieving total enteroscopy: a randomized, controlled trial. *Gastrointest Endosc*. 2011; 73:734–739. [PubMed: 21272875]
18. Godeschalk MF, Mensink PB, van Buuren HR, Kuipers EJ. Primary balloon-assisted enteroscopy in patients with obscure gastrointestinal bleeding: findings and outcome of therapy. *J Clin Gastroenterol*. 2010; 44:e195–200. [PubMed: 20505527]
19. Gay G, Delvaux M, Fassler I. Outcome of capsule endoscopy in determining indication and route for push-and-pull enteroscopy. *Endoscopy*. 2006; 38:49–58. [PubMed: 16429355]
20. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987; 40:373–383. [PubMed: 3558716]
21. Ramchandani M, Reddy DN, Gupta R, Lakhtakia S, Tandan M, et al. Diagnostic yield and therapeutic impact of single-balloon enteroscopy: series of 106 cases. *J Gastroenterol Hepatol*. 2009; 24:1631–1638. [PubMed: 19686408]
22. Agrawal JR, Travis AC, Morteale KJ, Silverman SG, Maurer R, et al. Diagnostic yield of dual-phase computed tomography enterography in patients with obscure gastrointestinal bleeding and a non-diagnostic capsule endoscopy. *J Gastroenterol Hepatol*. 2012; 27:751–759. [PubMed: 22098076]

23. Ge ZZ, Chen HM, Gao YJ, Liu WZ, Xu CH, et al. Efficacy of thalidomide for refractory gastrointestinal bleeding from vascular malformation. *Gastroenterology*. 2011; 141:1629–1637. e1621–1624. [PubMed: 21784047]
24. Junquera F, Feu F, Papo M, Videla S, Armengol JR, et al. A multicenter, randomized, clinical trial of hormonal therapy in the prevention of rebleeding from gastrointestinal angiodysplasia. *Gastroenterology*. 2001; 121:1073–1079. [PubMed: 11677198]
25. Arakawa D, Ohmiya N, Nakamura M, Honda W, Shirai O, et al. Outcome after enteroscopy for patients with obscure GI bleeding: diagnostic comparison between double-balloon endoscopy and videocapsule endoscopy. *Gastrointest Endosc*. 2009; 69:866–874. [PubMed: 19136098]
26. Heine GD, Hadithi M, Groenen MJ, Kuipers EJ, Jacobs MA, et al. Double-balloon enteroscopy: indications, diagnostic yield, and complications in a series of 275 patients with suspected small-bowel disease. *Endoscopy*. 2006; 38:42–48. [PubMed: 16429354]

Table 1

Baseline demographics and SBE findings in all 147 patients undergoing SBE 2008–2010

	Follow-up (n=110)	No follow- up (n=37)	P value
Age	70.6±11.3	69.3±16.4	0.08
Gender (female)	62 (56.4%)	16 (42.9%)	0.17
Charlson Comorbidity Index (CCI)	2.5 (0–14)	4 (0–12)	0.38
Presenting Symptom			
Overt GIB	55	25	0.73
Occult GIB	55	12	
SBE findings			
Abnormal SBE	76 (69.1%)	19 (51.4%)	0.01
VL	63	16	0.18
Neoplasm^	4	0	0.34
Gastroduodenal Ulcers	4	1	0.56
Inflammatory lesions of small bowel	5	2	0.68
Normal SBE	34	18	
SBE Directed Therapy	76 (69.1%)	13 (35.1%)	<0.001

[^] 1 adenoma, 1 carcinoid tumor, 1 GIST, 1 lymphoma

Table 2

Demographic and Clinical Characteristics of Patients With Follow-Up

	Total (n=110)	No Rebleeding (n=60)	Rebleeding (n=50)	P value
Age	70.6±11.3	72.1±11.3	68.8±10.98	0.08
Gender (female)	62 (56.4%)	37 (61.7%)	25 (50%)	0.17
Nadir Hemoglobin	7.6 (4.2–12)	7.7 (5.2–12)	7.2 (4.2–10.6)	0.50
Charlson Comorbidity Index (median, range)	2.8 (0–14)	2.5 (0–14)	3.4 (0–10)	0.38
Valvular Heart Disease	25 (22.7%)	8	17	0.1
Aspirin+/-Clopidogrel	50 (45.5%)	32	18	0.83
Warfarin	21 (19.1%)	12	9	0.82
Nature of Initial GI bleeding				
Overt	55 (50%)	29	26	0.86
Occult	55 (50%)	31	24	
Settings of SBE				
Outpatients	79	39	40 (50.6%)	0.08
Inpatients	31	21	10 (32.2%)	

Table 3**SBE Findings and Recurrent Bleeding During Long-Term Follow-Up**

	Total (n=110)	Percent with Recurrent OGIB	P value
SBE normal to depth of insertion	34	55.9% (19)	
Abnormal SBE	76	39.5% (30)	0.11
Anterograde SBE findings Proximal to Ligament of Treitz			
Cameron's ulcers/Peptic ulcers	4	0	
VL	8	37.5% (3)	
Anterograde SBE findings distal to Ligament of Treitz			
VL	53	49.1% (26)	
Tumor/Polyp	3	33.3% (1)*	
Inflammatory lesion	5	0	
Retrograde SBE			
VL	2	50% (1)	
Tumor/Polyp	1	0	
All VL found on SBE	63	47.6% (30)	0.47
All SBE patients	110	44.5% (49)	

* Patient who had jejunal polypectomy developed recurrent bleeding due to small bowel VLs 3 months after the initial SBE

Table 4

Long-term Rebleeding Rates after Deep Enteroscopy

Study			Follow-up duration (mean)	Findings	Rebleeding rate
Gerson	2009	DBE	30 months	Vascular lesions	45%
				Normal DBE	42%
				Overall	42%
Shinozaki	2010	DBE	29.7 months	Vascular lesions	60%
				Normal DBE	37%
				Overall	39%
May	2011	DBE	55 months	Vascular lesions	42%
				Normal DBE	N/A
				Overall	N/A
Samaha	2011	DBE	22.6 months	Vascular lesions	46%
				Normal DBE	N/A
				Overall	N/A
Kushnir	2012	SBE	23.9 months	Vascular lesions	48%
				Normal SBE	56%
				Overall	45%

N/A: not available