The role of endoscopy in the management of obscure GI bleeding

This is one of a series of statements discussing the use of GI endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy (ASGE) prepared this text. In preparing this guideline, we performed a search of the medical literature by using PubMed. Additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. Guidelines for appropriate use of endoscopy are based on a critical review of the available data and expert consensus at the time the guidelines were drafted. Further controlled clinical studies may be needed to clarify aspects of this guideline. This guideline may be revised as necessary to account for changes in technology, new data, or other aspects of clinical practice. The recommendations are based on reviewed studies and are graded on the strength of the supporting evidence (Table 1).[1] The strength of individual recommendations is based both upon the aggregate evidence quality and an assessment of the anticipated benefits and harms. Weaker recommendations are indicated by phrases such as "we suggest," whereas stronger recommendations are typically stated as "we recommend."

This guideline is intended to be an educational device to provide information that may assist endoscopists in providing care to patients. This guideline is not a rule and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment. Clinical decisions in any particular case involve a complex analysis of the patient's condition and available courses of action. Therefore, clinical considerations may lead an endoscopist to take a course of action that varies from these guidelines.

BACKGROUND

Obscure GI bleeding (OGIB) is defined as occult or overt bleeding of unknown origin that persists or recurs after an initial negative endoscopic evaluation including colonoscopy and EGD. Overt OGIB is defined as visible GI bleeding (eg, melena or hematochezia) and can be categorized further as active (ie, evidence of ongoing bleeding) versus inactive bleeding. Although there are no standard criteria for defining occult OGIB, for the purposes of this document, OGIB is designated as occult when there is no evidence of gross bleeding (eg, unexplained iron deficiency anemia suspected to be caused by GI blood loss).

Approximately 5% of GI bleeding occurs between the ligament of Treitz and the ileocecal valve.[2] Angiectasias of the small bowel account for 30% to 40% of OGIB and are the most common source in older patients.[3] Nonsteroidal anti-inflammatory drug enteropathy and inflammatory bowel disease have been associated with erosions, ulcers, and strictures of the small bowel and therefore are also causes of OGIB.[4,5] Other causes include tumors, which are considered the most common source of OGIB in patients <50 years old (eg, leiomyomas, carcinoid tumors, lymphomas, and adenocarcinomas),[6] Meckel's diverticula–associated ulceration (especially in younger patients),[7,8] radiation enteropathy,[9] Dieulafoy's lesions,[10] hemosuccus pancreaticus,[11] and small-bowel varices.[12-14]

OGIB may occur anywhere throughout the GI tract. Prior to evaluation of the small bowel, upper and lower GI tract endoscopies are often repeated in patients with OGIB because substantial initial endoscopic miss rates have been reported.[15,16] Newer endoscopic evaluation techniques for the small bowel include video capsule endoscopy (VCE) and deep enteroscopy. The diagnostic yield and therapeutic capabilities of these technologies have been compared with the conventional approaches of push enteroscopy (PE), intraoperative enteroscopy, and radiologic methods and show promise in producing superior yields. However, the most cost-effective approach to the management of patients with OGIB has not been fully determined. This guideline is an update of a prior ASGE document on the management of OGIB.[17] In this guideline, we describe the performance characteristics of various endoscopic and nonendoscopic tests available to evaluate patients with OGIB, followed by a suggested diagnostic approach.

DIAGNOSTIC TESTS FOR THE EVALUATION OF OGIB

EGD and colonoscopy

EGD is indicated for the initial evaluation of a suspected upper GI source of bleeding. Early endoscopic intervention has been associated with lower hospital cost; however, optimal timing after an episode of bleeding and the impact of early endoscopy on diagnostic yield have not been rigorously studied.[18] Repeat examination may yield a source even when the initial EGD is negative. For example, in studies of patients with OGIB that used small-bowel technologies, sus-

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TABLE 1. GRADE system for rating the quality of evidence for guidelines

Quality of evidence	Definition	Symbol
High quality	Further research is very unlikely to change our confidence in the estimate of effect.	⊕⊕⊕⊕
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.	⊕⊕⊕◯
Low quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.	⊕⊕◯◯
Very low quality	Any estimate of effect is very uncertain.	⊕◯◯◯

Adapted from the classification developed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group.[1]

pected sources of bleeding were found within the reach of a standard EGD in 2.8% (4/140)[19] and 4.7% (6/128)[20] of patients during VCE, in 26% (25/95)[15] of patients in studies that used PE, and in 13.1% (14/107)[21] of patients undergoing balloon-assisted enteroscopy (BAE). Examples of missed lesions in the upper GI tract include Cameron's erosions, peptic ulcerations, angiectasias, Dieulafoy's lesions, hemosuccus pancreaticus, and gastric antral vascular ectasias. Factors associated with an increased yield of repeat EGD include large hiatal hernias, hematemesis, and a history of nonsteroidal anti-inflammatory drug use.[22] Patients with upper GI mucosal lesions also may have other contributing causes of iron deficiency anemia, such as malabsorption.[23-27] Small-bowel biopsy to evaluate for celiac disease should be considered in patients with iron deficiency anemia and/or occult GI bleeding.[28] One prospective, controlled study in adults with iron deficiency anemia showed that 11.8% of these patients (11/93) had biopsy findings of celiac disease.[25]

In patients with OGIB, repeat colonoscopy should be considered when a clinical suspicion for missed lower colon lesions exists, although studies have reported variable yields in the detection of lower GI tract lesions when the colon is reinspected endoscopically. For example, lower GI lesions were found in 0 of 50 patients undergoing repeat colonoscopy prior to VCE [29] but in 10 of 35 patients (29%) undergoing retrograde BAE 1 week after a negative colonoscopy.[21] In patient populations in which colon cancers were discovered only on repeat examination, miss rates have been attributed to several factors including incomplete procedures and poor bowel preparation.[30]

Push enteroscopy

Push enteroscopy (PE) involves per oral endoscope insertion into the jejunum, without the assistance of balloons or spiral overtubes. The diagnostic yield for a bleeding source in the setting of OGIB is approximately 24% to 56%.[22,31-33] In a study of 63 patients, after exclusion of all lesions proximal to the ligament of Treitz, the diagnostic yield for PE was 41% in patients with recurrent overt OGIB, 33% in those with persistent overt OGIB, and 26% in those with occult OGIB.[34] PE allows not only for diagnosis and biopsy but also for therapeutic interventions, such as hemostasis. Decreased transfusion requirements and improvement in functional status 1 year after treatment have been demonstrated after PE.[35]

Video capsule endoscopy

VCE enables visualization of the entire small intestine but lacks the potential for therapeutic intervention. A detailed description of VCE can be found in a separate ASGE document.[36] A meta-analysis of 14 prospective studies including 396 patients with OGIB showed a higher yield for clinically significant lesions with VCE (56%) than with PE (26%) or small-bowel follow-through (6%).[37] Compared with the criterion standard of intraoperative enteroscopy for detecting a bleeding source, VCE had a sensitivity of 95% and specificity of 75% in a prospective, two-center study of 47 patients.[38] In comparison with CT angiography and standard angiography, VCE detected more bleeding source lesions (72% with VCE vs 24% with CTA and 56% with angiography).[39] High diagnostic yields (91.9%) for urgently performed VCE (ie, within 48 hours after admission) in patients with mild to moderate acute overt OGIB suggest that early intervention with VCE may enhance diagnostic effectiveness.

Benefits of VCE include the noninvasive nature of the test, patient acceptance, safety, and diagnostic yield. Limitations of VCE include inability to provide therapy or precisely locate a lesion, false-positive results, the potential for erratic passage resulting in missed lesions, and limited battery life of the equipment causing incomplete studies. The primary risk of VCE is retention, occurring in 1.4% of VCE examinations in one large study.[40] Further discussion about the contraindications to VCE and interactions between implanted electronic devices and VCE can be found in other ASGE Technology Status Evaluation reports.[36,41]

If significant lesions are detected on VCE, the patient should be referred for specific management of these findings. Rebleeding rates after a negative VCE study are generally low (6%-11%).[42,43] If the VCE study fails to identify the cause of OGIB, a second VCE study may be considered, although outcomes have been mixed. In a prospective study of 76 patients with persistent OGIB and a nondiagnostic VCE, a "second look" VCE was positive in 49% of patients.[44] The second VCE was more likely to be diagnostic when a patient's clinical course changed from occult to overt bleeding or if the hemoglobin level dropped ≥4 g/dL. One small, prospective study of 20

patients with iron deficiency anemia[45] found that 35% of second VCE studies showed positive or suspected findings, and 10% resulted in changed management.

Deep enteroscopy

Deep enteroscopy encompasses both BAE (ie, single and double balloon systems) and spiral enteroscopy.[46-48] Total enteroscopy may be achieved through a combination of antegrade and retrograde approaches.[46] A detailed discussion of BAE can be found in an ASGE Technology Evaluation Status report.[49]

In multiple large studies of patients with OGIB who underwent BAE, the diagnostic yield ranged from 43% to 81%.[50-56] Treatment success rates of between 43% and 84% have been reported.[51-55] Few studies have evaluated a combined antegrade and retrograde approach.[52-55] Multiple studies have been conducted to compare BAE with PE and VCE. In one controlled, prospective trial of 52 patients with OGIB, BAE was superior to PE in length of small bowel visualized (230 cm vs 80 cm, $P < .0001$) and diagnostic yield (63% vs 44%, $P < .0001$).[31]

A meta-analysis of 11 studies comparing the yield of VCE and BAE, including 375 patients with small-bowel disease, reported comparable diagnostic yields (60% vs 57%, respectively). The pooled yield for angiectasias in the 350 patients with OGIB was identical, with 24% for both VCE and BAE.[57] A more recent retrospective study of 162 patients with OGIB also suggested no significant difference in overall diagnostic yield between VCE (54%) and BAE (64%)[56] Similar results were found in another meta-analysis. In this study, a subanalysis of 191 patients undergoing only antegrade or retrograde BAE indicated a significantly higher yield of VCE vs BAE (62% vs 50%, $P < .05$). However, when both antegrade and retrograde BAEs were performed in 24 patients, the yield of BAE was higher than that of VCE (88% vs 46%, $P < .01$).[58] Finally, in a retrospective study investigating the role of BAE prior to intraoperative endoscopy for those in whom BAE identified a source (53/56 patients), subsequent intraoperative endoscopy was negative in only one patient.[59]

A modeled cost-minimization analysis of the management of occult OGIB proposed BAE as the most cost-effective initial test after standard endoscopy if the goal is treatment or definitive diagnosis.[60] Another model suggested that initial BAE was a cost-effective approach for patients with OGIB who likely have angiectasias in the small bowel accessible with a single antegrade approach.[61] Spiral enteroscopy, in which a specialized spiral overtube is placed over a pediatric colonoscope, has been recently described.[62] However, comparative studies regarding existing deep enteroscopy techniques are lacking.

Radiographic contrast studies of the small bowel

Until recently, small-bowel follow-through was routinely used to screen the small intestine for a potential bleeding source. The yield of small-bowel follow-through in the evaluation of OGIB is extremely low (0%-5.6%),[63,64] and a comparison of small-bowel follow-through and PE in 40 patients demonstrated a superior yield of PE (2.5% vs 35%, respectively).[65] Enteroclysis allows more detailed visualization of the small bowel, with utility in detection of inflammatory bowel disease and neoplasm in patients with OGIB.[66] However, enteroclysis has not been shown to be useful in the detection of angiectasia, and it identifies a bleeding source in only 8% of patients with negative PEs.[67] In patients with active bleeding, the use of contrast material may complicate subsequent evaluation with endoscopy or other radiologic imaging tests. Both small-bowel follow-through and enteroclysis should be considered of limited value in the evaluation of GI bleeding.

Nuclear scans

Radioisotope bleeding scans may be helpful in cases of overt OGIB if the bleeding rate is at least 0.1 to 0.4 mL/minute.[68] The technetium 99m-labeled red blood cell scan is used most commonly in the actively bleeding patient in which no source has been identified on EGD or colonoscopy. These scans can aid in the localization of bleeding that can then be verified with repeat endoscopy, angiography, or surgery. An early blush appears to be more accurate than delayed positivity in lower GI hemorrhage.[69] Although sensitive, nuclear medicine scans can identify only a general area of bleeding and are very limited in terms of directing treatment. Results from studies of technetium-labeled red blood cell scintigraphy vary widely and may reflect differences in patient selection and timing of the study in relation to clinical presentation. In one study of 103 patients with OGIB, scintigraphy failed to localize hemorrhage in 85% of cases and was a poor predictor of a positive angiographic study.[70] In another retrospective study of 92 patients with OGIB, 25% had a definitive bleeding source found and confirmed with further diagnostic procedures.[68] In pediatric patients and young adults, Meckel's scanning is a useful test for overt OGIB, with a sensitivity ranging between 50% and 91% for ectopic gastric mucosa.[8]

Angiography

Angiography also may be helpful in the evaluation of overt OGIB if the bleeding rate is >0.5 mL/minute.[71] Although technically less sensitive than nuclear scans, it is more effective at localizing the bleeding site.[72] There are limited data on the diagnostic yield of angiography in OGIB. Reported yields range from 27% to 77% in lower GI bleeding.[73] There is some evidence that if the initial angiogram is negative, a repeat study may be of benefit.[74] Angiography carries the potential for therapy, including superselective mesenteric embolization.[75,76]

CT imaging

CT enterography is a noninvasive imaging technique that uses neutral intraluminal and intravenous contrast to

evaluate the small bowel and has been particularly useful in enhancement of the small-intestine wall in inflammatory bowel disease. Recent improvements from single phase (for inflammatory bowel disease) to multiphasic imaging allow detection of a vascular blush, which is important for recognition of small vascular lesions. Initial experience with 64-section, multiphase CT enterography at one center reported successful identification of a bleeding source in 45% of 22 outpatients with OGIB, including 3 lesions that were missed on VCE.[77] In a study of 26 patients with massive GI bleeding, a multiple-detector CT had an accuracy of 89% and positive predictive value of 95%.[78] The location of lesions corresponded exactly to that of active bleeding on angiograms in all patients.

CT angiography visualizes extravasation of contrast medium into the intestinal lumen in order to identify the source of OGIB. In one study of 18 patients, CT angiography was found to be easier and faster for localizing OGIB than conventional angiography and useful as a guide to subsequent selective conventional angiography.[79]

Intraoperative enteroscopy

Intraoperative enteroscopy during laparotomy or laparoscopy is typically used as a last resort in patients with OGIB requiring multiple transfusions and/or repeated hospitalizations.[80] Endoscopic evaluation can be performed orally, rectally, or through enterotomies at the time of surgery. This procedure appears to be safe and effective,[81] although there are no controlled trials comparing intraoperative enteroscopy with other therapeutic procedures for OGIB. Early studies, before the advent of BAE and VCE, have shown diagnostic yields of intraoperative enteroscopy in GI bleeding to be between 58% and 82%.[82-85]

The role of intraoperative enteroscopy in coordination with VCE was evaluated in a recent study of 18 patients with OGIB. In the 15 patients with lesions on VCE, intraoperative enteroscopy yielded treatment in 13 (87%), whereas in the 3 negative VCE studies, the intraoperative enteroscopy result was normal, suggesting an important directive role for VCE.[86]

DIAGNOSTIC APPROACH TO PATIENTS WITH OGIB

The diagnostic approach to patients with OGIB depends upon clinical factors, such as the age of the patient, quality of the prior endoscopic evaluation, and the overt or occult status of the bleeding. Clinical clues, such as nasogastric tube aspirates and the nature of the bleeding (eg, melena vs hematochezia) can help direct the choice of endoscopic tests. In addition, local availability of procedures, patient preferences, physician expertise, risks, and costs are also important determinants of management. Resuscitation is key to the management of all patients with GI bleeding.[87] Patients on antithrombotic therapy should be managed according to recent ASGE guidelines.[88] A suggested algorithm for management is shown in Figures 1 and 2.

Overt OGIB

Active overt OGIB. If the clinical presentation is compatible with upper GI bleeding (eg, hematemesis or blood in the nasogastric tube aspirate), then urgent EGD should be performed. Otherwise, recommended diagnostic options include PE, repeat colonoscopy, VCE, and tagged red blood cell scintigraphy. Other options include deep enteroscopy, CT enterography, or CT angiography. Because these tests are complementary, a combination may be required. Furthermore, in patients with surgically altered anatomy in whom portions of the GI tract are bypassed (eg, Roux-en-Y gastrojejunostomy), deep enteroscopy is the preferred endoscopic modality to assess the excluded luminal segment, because other approaches cannot reach these areas.[89,90] For those patients who present with massive bleeding, endoscopy with therapeutic capability (eg, PE or colonoscopy) or referral for angiography are recommended. If these tests are negative, then management as described for inactive overt OGIB is suggested.

Inactive overt OGIB. For those patients with a history of recent overt OGIB who now have no evidence of ongoing bleeding (eg, normal-appearing stools), recommended diagnostic options include VCE, deep enteroscopy, PE, and/or colonoscopy. Because these tests are complementary, a combination may be required. Other options include CT enterography or CT angiography. If these tests are negative, and bleeding recurs, then provocative testing (as described later) or intraoperative enteroscopy may be appropriate.

Occult OGIB

In patients with occult OGIB, options include repeat endoscopy (ie, EGD and colonoscopy) and evaluation of the small bowel. In some situations, a trial of empiric iron supplementation prior to further diagnostic work-up may be appropriate. EGD should be considered when an upper GI lesion is suspected, such as in patients with risk factors for mucosal disease caused by nonsteroidal anti-inflammatory drug use, or if details of the prior EGD are uncertain. Repeat colonoscopy should be considered when the quality of the bowel preparation on the initial examination was suboptimal or when other questions about the quality of the examination exist. Additionally, when there is clinical suspicion for missed colonic lesions, repeat colonoscopy also may be performed.[30]

To evaluate the small bowel for occult OGIB, VCE is recommended as the first diagnostic test if no contraindications exist. Other options for small-bowel examination include deep enteroscopy or PE. Barium radiography studies, such as small-bowel follow-through and enteroclysis, and cross-sectional imaging, such as single-phase

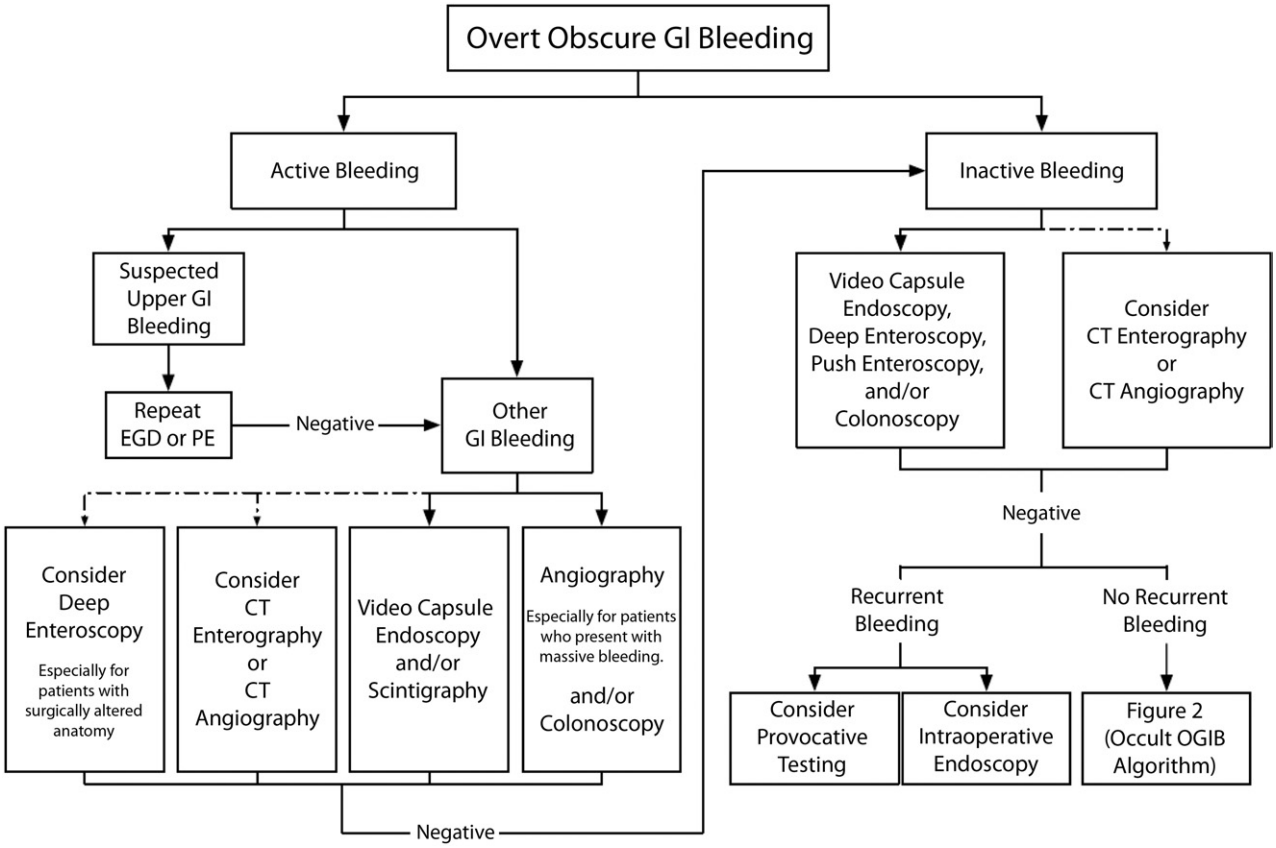

Figure 1. Suggested diagnostic approach to **overt** obscure GI bleeding. Dashed arrows indicate less-preferred options. Positive test results should direct specific therapy. Because diagnostic tests can be complementary, more than one test may be needed, and the first-line test may be based upon institutional expertise and availability. *PE,* push enteroscopy; *OGIB,* obscure GI bleeding.

CT enterography, have low diagnostic yields. Several authors have suggested initial VCE followed by therapeutic BAE, if positive, as the best strategy for increased yield and improved treatment success.[91-94]

If VCE is performed, and a culprit lesion is found, appropriate endoscopic, angiographic, medical, or surgical intervention should be instituted. If VCE is negative, the patient's clinical status should dictate the next step. Stable patients may be observed without further evaluation. For patients who need further work-up or have recurrent bleeding, a selection of diagnostic modalities exists. Patients who did not have a second-look endoscopy may, at this point, benefit from repeat EGD and/or colonoscopy. A repeat VCE also may be informative, particularly in patients whose presentations change from occult to overt bleeding or those with decreases in hemoglobin levels of ≥4 g/dL.[44]

Provocative testing

To avoid false-negative studies, vasodilators (eg, tolazoline or nitroglycerin), anticoagulants (eg, heparin), and/or fibrinolytics (eg, urokinase or streptokinase) have been used to induce bleeding during bleeding scans, angiography, or endoscopic studies for the evaluation of OGIB.[95-98] Although some investigators have reported an increased diagnostic yield,[95] others have found a more limited benefit[96] and have questioned the cost-effectiveness and safety of this approach.[97] To determine the effect on predictive value, a study of 18 patients with OGIB found that heparinization improved the diagnostic yield of angiography from 33% to 67% with no reported complications.[98] There is currently insufficient evidence to support or refute the effectiveness and safety of provocative testing in the evaluation of OGIB.

THERAPEUTIC APPROACH TO PATIENTS WITH OGIB

Therapy for OGIB depends on the etiology of the bleeding. Lesions found within the reach of a standard endoscope can be treated with appropriate therapy such as electrocautery, argon plasma coagulation, injection therapy, mechanical hemostasis (eg, hemoclips or bands), or a combination of these techniques. More distal vascular lesions, such as angiectasias, may be approached for therapy via PE or deep enteroscopy, depending upon location. There is evidence that treatment has a positive impact on clinical outcome, by decreasing blood loss and need

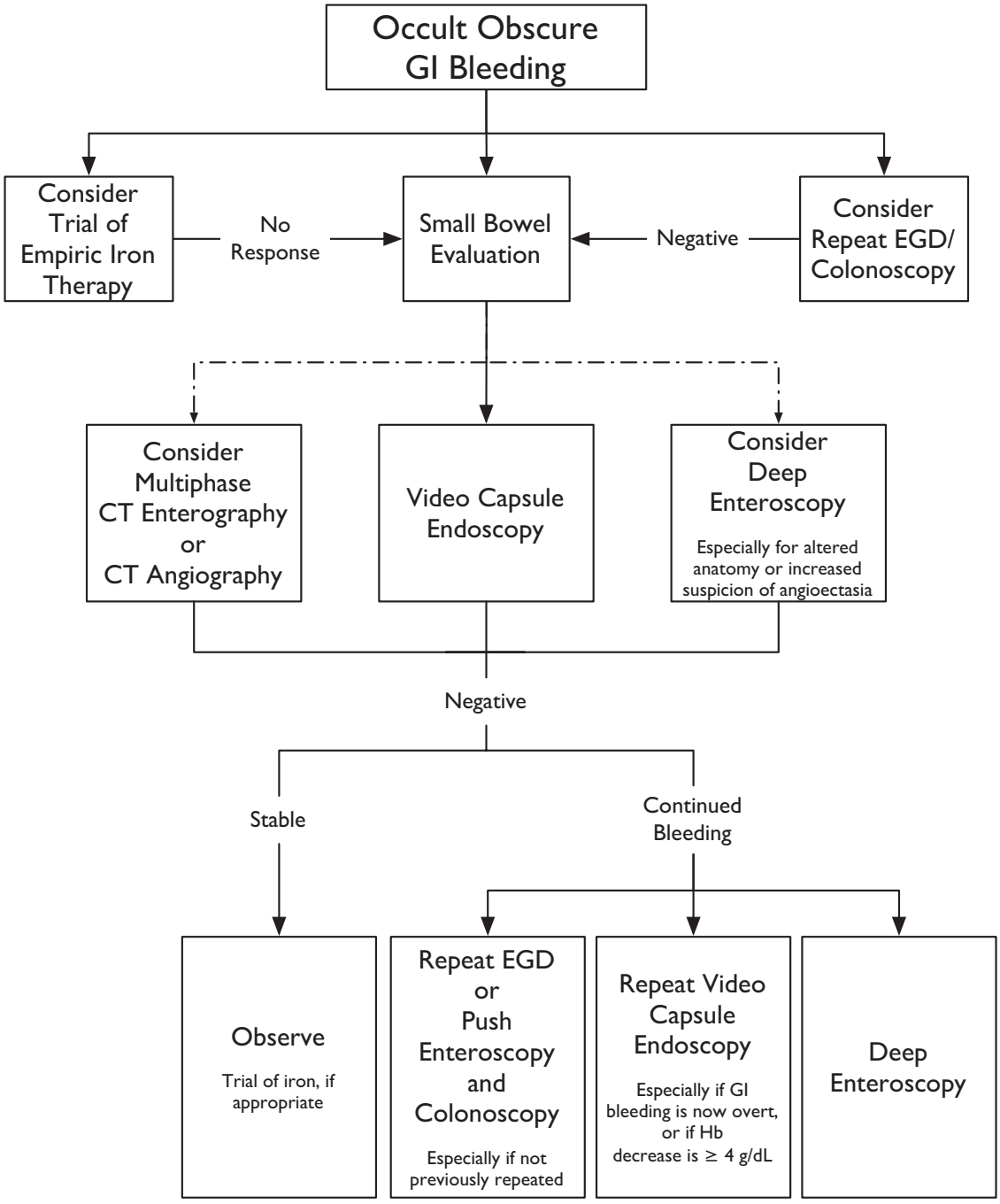

Figure 2. Suggested diagnostic approach to **occult** obscure GI bleeding. Dashed arrows indicate less-preferred options. Positive test results should direct specific therapy. Because diagnostic tests can be complementary, more than one test may be needed, and the first-line test may be based upon institutional expertise and availability. *Hb,* hemoglobin.

for blood transfusions.[99,100] Masses or tumors likely require surgical intervention or intraoperative enteroscopy, and management of massive bleeding should be coordinated with surgery and interventional radiology. Oral or intravenous iron supplementation or transfusions may be required in some patients. Hormonal therapy for angiectasias is controversial but has largely been abandoned because of lack of beneficial effect.[101-104] Long-acting octreotide has shown some benefit in eliminating the need for transfusions and iron supplementation in patients with chronic blood loss from angiectasias,[105,106] but this has not been extensively studied.

RECOMMENDATIONS

1. After appropriate resuscitation, we recommend emergent endoscopy or angiography in patients with massive OGIB. ⊕⊕○○

2. We recommend urgent EGD in patients with active overt OGIB and a clinical presentation suggestive of upper GI bleeding. ⊕⊕⊕○ For those with signs or symptoms of lower GI bleeding, we suggest repeating colonoscopy. ⊕⊕○○ Otherwise, recommended diagnostic options include PE, VCE, and tagged red blood cell scintigraphy.
3. For those patients with inactive overt OGIB, we suggest VCE, deep enteroscopy, PE, and/or colonoscopy. ⊕⊕○○
4. In patients with occult OGIB and a high clinical suspicion for an upper GI lesion, we suggest repeating EGD before small-bowel evaluation. ⊕⊕○○ For those with a suspected lower GI lesion, we suggest repeating colonoscopy prior to small-bowel evaluation. ⊕⊕○○ In the absence of localizing signs or symptoms, we recommend small-bowel evaluation. ⊕⊕⊕○
5. We recommend VCE as the first-line diagnostic tool for evaluation of the small bowel in patients with OGIB. ⊕⊕⊕○
6. We suggest that in select circumstances (eg, where there is a high level of suspicion of small-bowel angiectasias or in patients with surgically altered anatomy), deep enteroscopy may be considered as the initial small-bowel diagnostic procedure in patients with OGIB. ⊕⊕○○
7. We recommend that patients with occult OGIB and a negative VCE evaluation who remain clinically stable be treated with iron therapy if evidence of iron deficiency is present. ⊕⊕⊕○
8. We suggest that, in patients with negative VCEs and continued bleeding, repeat VCE be considered, particularly if the clinical state changes from obscure to overt bleeding or if the hemoglobin level drops by ≥4 g/dL. ⊕⊕○○
9. We suggest that small-bowel follow-through and enteroclysis have a limited role in the evaluation of OGIB, given their low yields for identifying lesions. ⊕⊕○○

Abbreviations: ASGE, American Society for Gastrointestinal Endoscopy; BAE, balloon-assisted enteroscopy; OGIB, obscure GI bleeding; PE, push enteroscopy; VCE, video capsule endoscopy.

REFERENCES

1. Guyatt G, Oxman A, Vist G, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. Br Med J 2008;336:924-6.
2. Katz LB. The role of surgery in occult gastrointestinal bleeding. Semin Gastrointest Dis 1999;10:78-81.
3. Foutch PG. Angiodysplasia of the gastrointestinal tract. Am J Gastroenterol 1993;88:807-18.
4. Kwo PY, Tremaine WJ. Nonsteroidal anti-inflammatory drug-induced enteropathy: case discussion and review of the literature. Mayo Clin Proc 1995;70:55-61.
5. Lang J, Price AB, Levi AJ, et al. Diaphragm disease: pathology of disease of the small intestine induced by non-steroidal anti-inflammatory drugs. J Clin Pathol 1988;41:516-26.
6. Lewis BS, Kornbluth A, Waye JD. Small bowel tumours: yield of enteroscopy. Gut 1991;32:763-5.
7. Bartram CI, Amess JA. The diagnosis of Meckel's diverticulum by small bowel enema in the investigation of obscure intestinal bleeding. Br J Surg 1980;67:417-8.
8. Kiratli P, Aksoy T, Bozkurt M, et al. Detection of ectopic gastric mucosa using 99mTc pertechnetate: review of the literature. Ann Nucl Med 2009;23:97-105.
9. Taverner D, Talbot IC, Carr-Locke DL, et al. Massive bleeding from the ileum: a late complication of pelvic radiotherapy. Am J Gastroenterol 1982;77:29-31.
10. Blecker D, Bansal M, Zimmerman RL, et al. Dieulafoy's lesion of the small bowel causing massive gastrointestinal bleeding: two case reports and literature review. Am J Gastroenterol 2001;96:902-5.
11. Risti B, Marincek B, Jost R, et al. Hemosuccus pancreaticus as a source of obscure upper gastrointestinal bleeding: three cases and literature review. Am J Gastroenterol 1995;90:1878-80.
12. Yuki N, Kubo M, Noro Y, et al. Jejunal varices as a cause of massive gastrointestinal bleeding. Am J Gastroenterol 1992;87:514-7.
13. Traina M, Tarantino I, Barresi L, et al. Variceal bleeding from ileum identified and treated by single balloon enteroscopy. World J Gastroenterol 2009;15:1904-5.
14. Kodama M, Uto H, Numata M, et al. Endoscopic characterization of the small bowel in patients with portal hypertension evaluated by double balloon endoscopy. J Gastroenterol 2008;43:589-96.
15. Zaman A, Katon RM. Push enteroscopy for obscure gastrointestinal bleeding yields a high incidence of proximal lesions within reach of a standard endoscope. Gastrointest Endosc 1998;47:372-6.
16. Descamps C, Schmit A, Van Gossum A. "Missed" upper gastrointestinal tract lesions may explain "occult" bleeding. Endoscopy 1999;31:452-5.
17. Leighton J, Goldstein J, Hirota W, et al. Obscure gastrointestinal bleeding. Gastrointest Endosc 2003;58:650-5.
18. Lee JG. Endoscopy-based triage significantly reduces hospitalization rates and costs of treating upper GI bleeding: a randomized controlled trial. Gastrointest Endosc 1999;50:755-61.
19. Kitiyakara T, Selby W. Non-small-bowel lesions detected by capsule endoscopy in patients with obscure GI bleeding. Gastrointest Endosc 2005;62:234-8.
20. Sidhu R, Sanders DS, McAlindon ME. Does capsule endoscopy recognise gastric antral vascular ectasia more frequently than conventional endoscopy? J Gastrointestin Liver Dis 2006;15:375-7.
21. Fry LC, Bellutti M, Neumann H, et al. Incidence of bleeding lesions within reach of conventional upper and lower endoscopes in patients undergoing double-balloon enteroscopy for obscure gastrointestinal bleeding. Aliment Pharmacol Ther 2009;29:342-9.
22. Chak A, Koehler MK, Sundaram SN, et al. Diagnostic and therapeutic impact of push enteroscopy: analysis of factors associated with positive findings. Gastrointest Endosc 1998;47:18-22.
23. Bampton PA, Holloway RH. A prospective study of the gastroenterological causes of iron deficiency anaemia in a general hospital. Aust N Z J Med 1996;26:793-9.
24. Kepczyk T, Kadakia SC. Prospective evaluation of gastrointestinal tract in patients with iron-deficiency anemia. Dig Dis Sci 1995;40:1283-9.
25. Ackerman Z, Eliakim R, Stalnikowicz R, et al. Role of small bowel biopsy in the endoscopic evaluation of adults with iron deficiency anemia. Am J Gastroenterol 1996;91:2099-102.
26. Harewood G, Holub J, Lieberman D. Variation in small bowel biopsy performance among diverse endoscopy settings: results from a national endoscopic database. Am J Gastroenterol 2004;99:1790-4.
27. Grisolano S, Oxentenko A, Murray J, et al. The usefulness of routine small bowel biopsies in evaluation of iron deficiency anemia. J Clin Gastroenterol 2004;38:756-60.
28. Fine KD. The prevalence of occult gastrointestinal bleeding in celiac sprue. N Engl J Med 1996;334:1163-7.
29. Gilbert D, O'Malley S, Selby W. Are repeat upper gastrointestinal endoscopy and colonoscopy necessary within six months of capsule en-

doscopy in patients with obscure gastrointestinal bleeding? J Gastroenterol Hepatol 2008;23:1806-9.
30. Leaper M, Johnston MJ, Barclay M, et al. Reasons for failure to diagnose colorectal carcinoma at colonoscopy. Endoscopy 2004;36:499-503.
31. May A, Nachbar L, Schneider M, et al. Prospective comparison of push enteroscopy and push-and-pull enteroscopy in patients with suspected small-bowel bleeding. Am J Gastroenterol 2006;101:2016-24.
32. de Leusse A, Vahedi K, Edery J, et al. Capsule endoscopy or push enteroscopy for first-line exploration of obscure gastrointestinal bleeding? Gastroenterology 2007;132:855-62; quiz 1164.
33. Sidhu R, McAlindon M, Kapur K, et al. Push enteroscopy in the era of capsule endoscopy. J Clin Gastroenterol 2008;42:54-8.
34. Lara LF, Bloomfeld RS, Pineau BC. The rate of lesions found within reach of esophagogastroduodenoscopy during push enteroscopy depends on the type of obscure gastrointestinal bleeding. Endoscopy 2005;37: 745-50.
35. Vakil N, Huilgol V, Khan I. Effect of push enteroscopy on transfusion requirements and quality of life in patients with unexplained gastrointestinal bleeding. Am J Gastroenterol 1997;92:425-8.
36. Mishkin D, Chuttani R, Croffie J, et al. ASGE Technology Status Evaluation Report: wireless capsule endoscopy. Gastrointest Endosc 2006;63: 539-45.
37. Triester S, Leighton J, Leontiadis G, et al. A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with obscure gastrointestinal bleeding. Am J Gastroenterol 2005;100:2407-18.
38. Hartmann D, Schmidt H, Bolz G, et al. A prospective two-center study comparing wireless capsule endoscopy with intraoperative enteroscopy in patients with obscure GI bleeding. Gastrointest Endosc 2005; 61:826-32.
39. Saperas E, Dot J, Videla S, et al. Capsule endoscopy versus computed tomographic or standard angiography for the diagnosis of obscure gastrointestinal bleeding. Am J Gastroenterol 2007;102:731-7.
40. Li F, Gurudu S, De Petris G, et al. Retention of the capsule endoscope: a single-center experience of 1000 capsule endoscopy procedures. Gastrointest Endosc 2008;68:174-80.
41. Petersen B, Hussain N, Marine J, et al. Endoscopy in patients with implanted electronic devices. Gastrointest Endosc 2007;65:561-8.
42. Macdonald J, Porter V, McNamara D. Negative capsule endoscopy in patients with obscure GI bleeding predicts low rebleeding rates. Gastrointest Endosc 2008;68:1122-7.
43. Lai L, Wong GLH, Chow DKL, et al. Long-term follow-up of patients with obscure gastrointestinal bleeding after negative capsule endoscopy. Am J Gastroenterol 2006;101:1224-8.
44. Viazis N, Papaxoinis K, Vlachogiannakos J, et al. Is there a role for second-look capsule endoscopy in patients with obscure GI bleeding after a nondiagnostic first test? Gastrointest Endosc 2009;69:850-6.
45. Bar-Meir S, Eliakim R, Nadler M, et al. Second capsule endoscopy for patients with severe iron deficiency anemia. Gastrointest Endosc 2004; 60:711-3.
46. Yamamoto H, Sekine Y, Sato Y, et al. Total enteroscopy with a nonsurgical steerable double-balloon method. Gastrointest Endosc 2001;53: 216-20.
47. Tsujikawa T, Saitoh Y, Andoh A, et al. Novel single-balloon enteroscopy for diagnosis and treatment of the small intestine: preliminary experiences. Endoscopy 2008;40:11-5.
48. Akerman P, Agrawal D, Chen W, et al. Spiral enteroscopy: a novel method of enteroscopy by using the Endo-Ease Discovery SB overtube and a pediatric colonoscope. Gastrointest Endosc 2009;69:327-32.
49. DiSario J, Petersen B, Tierney W, et al. Enteroscopes. Gastrointest Endosc 2007;66:872-80.
50. Zhi F-c, Yue H, Jiang B, et al. Diagnostic value of double balloon enteroscopy for small-intestinal disease: experience from China. Gastrointest Endosc 2007;66:S19-21.
51. Zhong J, Ma T, Zhang C, et al. A retrospective study of the application on double-balloon enteroscopy in 378 patients with suspected small-bowel diseases. Endoscopy 2007;39:208-15.
52. Cazzato IA, Cammarota G, Nista EC, et al. Diagnostic and therapeutic impact of double-balloon enteroscopy (DBE) in a series of 100 patients with suspected small bowel diseases. Dig Liver Dis 2007;39:483-7.
53. Nakamura M, Niwa Y, Ohmiya N, et al. Preliminary comparison of capsule endoscopy and double-balloon enteroscopy in patients with suspected small-bowel bleeding. Endoscopy 2006;38:59-66.
54. Mehdizadeh S, Ross A, Gerson L, et al. What is the learning curve associated with double-balloon enteroscopy? technical details and early experience in 6 U.S. tertiary care centers. Gastrointest Endosc 2006;64: 740-50.
55. Manabe N, Tanaka S, Fukumoto A, et al. Double-balloon enteroscopy in patients with GI bleeding of obscure origin. Gastrointest Endosc 2006;64:135-40.
56. Arakawa D, Ohmiya N, Nakamura M, et al. Outcome after enteroscopy for patients with obscure GI bleeding: diagnostic comparison between double-balloon endoscopy and videocapsule endoscopy. Gastrointest Endosc 2009;69:866-74.
57. Pasha S, Leighton J, Das A, et al. Double-balloon enteroscopy and capsule endoscopy have comparable diagnostic yield in small-bowel disease: a meta-analysis. Clin Gastroenterol Hepatol 2008;6:671-6.
58. Chen X, Ran Z-H, Tong J-L. A meta-analysis of the yield of capsule endoscopy compared to double-balloon enteroscopy in patients with small bowel diseases. World J Gastroenterol 2007;13:4372-8.
59. Lin M-B, Yin L, Li J-W, et al. Double-balloon enteroscopy reliably directs surgical intervention for patients with small intestinal bleeding. World J Gastroenterol 2008;14:1936-40.
60. Somsouk M, Gralnek I, Inadomi J. Management of obscure occult gastrointestinal bleeding: a cost-minimization analysis. Clin Gastroenterol Hepatol 2008;6:661-70.
61. Gerson L, Kamal A. Cost-effectiveness analysis of management strategies for obscure GI bleeding. Gastrointest Endosc 2008;68:920-36.
62. Buscaglia JM, Dunbar KB, Okolo PI, et al. The spiral enteroscopy training initiative: results of a prospective study evaluating the Discovery SB overtube device during small bowel enteroscopy (with video). Endoscopy 2009;41:194-9.
63. Fried AM, Poulos A, Hatfield DR. The effectiveness of the incidental small-bowel series. Radiology 1981;140:45-6.
64. Rabe FE, Becker GJ, Besozzi MJ, et al. Efficacy study of the small-bowel examination. Radiology 1981;140:47-50.
65. Cellier C, Tkoub M, Gaudric M, et al. Comparison of push-type endoscopy and barium transit study of the small intestine in digestive bleeding and unexplained iron-deficiency anemia. Gastroenterol Clin Biol 1998;22:491-4.
66. Korman U, Kantarci F, Selçuk D, et al. Enteroclysis in obscure gastrointestinal system hemorrhage of small bowel origin. Turk J Gastroenterol 2003;14:243-9.
67. Willis JR, Chokshi HR, Zuckerman GR, et al. Enteroscopy-enteroclysis: experience with a combined endoscopic-radiographic technique. Gastrointest Endosc 1997;45:163-7.
68. Brunnler T, Klebl F, Mundorff S, et al. Significance of scintigraphy for the localisation of obscure gastrointestinal bleedings. World J Gastroenterol 2008;14:5015-9.
69. Ng DA, Opelka FG, Beck DE, et al. Predictive value of technetium Tc 99m-labeled red blood cell scintigraphy for positive angiogram in massive lower gastrointestinal hemorrhage. Dis Colon Rectum 1997; 40:471-7.
70. Voeller GR, Bunch G, Britt LG. Use of technetium-labeled red blood cell scintigraphy in the detection and management of gastrointestinal hemorrhage. Surgery 1991;110:799-804.
71. Nusbaum M, Baum S, Blakemore WS. Clinical experience with the diagnosis and management of gastrointestinal hemorrhage by selective mesenteric catheterization. Ann Surg 1969;170:506-14.
72. Rollins ES, Picus D, Hicks ME, et al. Angiography is useful in detecting the source of chronic gastrointestinal bleeding of obscure origin. AJR Am J Roentgenol 1991;156:385-8.
73. Zuckerman GR, Prakash C. Acute lower intestinal bleeding: part I: clinical presentation and diagnosis. Gastrointest Endosc 1998;48:606-17.

74. Lau WY, Ngan H, Chu KW, et al. Repeat selective visceral angiography in patients with gastrointestinal bleeding of obscure origin. Br J Surg 1989;76:226-9.
75. Tan K-K, Wong D, Sim R. Superselective embolization for lower gastrointestinal hemorrhage: an institutional review over 7 years. World J Surg 2008;32:2707-15.
76. Funaki B. Superselective embolization of lower gastrointestinal hemorrhage: a new paradigm. Abdom Imaging 2004;29:434-8.
77. Huprich J, Fletcher J, Alexander J, et al. Obscure gastrointestinal bleeding: evaluation with 64-section multiphase CT enterography: initial experience. Radiology 2008;246:562-71.
78. Yoon W, Jeong Y, Shin S, et al. Acute massive gastrointestinal bleeding: detection and localization with arterial phase multi-detector row helical CT. Radiology 2006;239:160-7.
79. Ettorre GC, Francioso G, Garribba AP, et al. Helical CT angiography in gastrointestinal bleeding of obscure origin. AJR Am J Roentgenol 1997;168:727-31.
80. Cave DR, Cooley JS. Intraoperative enteroscopy. Indications and techniques. Gastrointest Endosc Clin N Am 1996;6:793-802.
81. Lau WY, Wong SY, Yuen WK, et al. Intraoperative enteroscopy for bleeding angiodysplasias of small intestine. Surg Gynecol Obstet 1989; 168:341-4.
82. Ress AM, Benacci JC, Sarr MG. Efficacy of intraoperative enteroscopy in diagnosis and prevention of recurrent, occult gastrointestinal bleeding. Am J Gastroenterol 1992;163:94-8; discussion 98.
83. Lau WY, Yuen WK, Chu KW, et al. Obscure bleeding in the gastrointestinal tract originating in the small intestine. Surg Gynecol Obstet 1992; 174:119-24.
84. Zaman A, Sheppard B, Katon RM. Total peroral intraoperative enteroscopy for obscure GI bleeding using a dedicated push enteroscope: diagnostic yield and patient outcome. Gastrointest Endosc 1999;50: 506-10.
85. Douard R, Wind P, Panis Y, et al. Intraoperative enteroscopy for diagnosis and management of unexplained gastrointestinal bleeding. Am J Surg 2000;180:181-4.
86. Douard R, Wind P, Berger A, et al. Role of intraoperative enteroscopy in the management of obscure gastrointestinal bleeding at the time of video-capsule endoscopy. Am J Surg 2009;198:6-11.
87. Adler D, Leighton J, Davila R, et al. ASGE guideline: the role of endoscopy in acute non-variceal upper-GI hemorrhage. Gastrointest Endosc 2004;60:497-504.
88. Anderson MA, Ben-Menachem T, et al. ASGE guideline: the management of Antithrombotic agents for endoscopic procedures. Gastrointest Endosc 2009;70:1060-70.
89. Kim DH, Byeon J-S, Lee SK, et al. Usefulness of double balloon endoscopy in patients with surgically distorted intestinal anatomy. J Clin Gastroenterol 2009 March 3 [Epub ahead of print].
90. Baron T. Double-balloon enteroscopy to facilitate retrograde PEG placement as access for therapeutic ERCP in patients with long-limb gastric bypass. Gastrointest Endosc 2006;64:973-4.
91. Kamalaporn P, Cho S, Basset N, et al. Double-balloon enteroscopy following capsule endoscopy in the management of obscure gastrointestinal bleeding: outcome of a combined approach. Can J Gastroenterol 2008;22:491-5.
92. Fujimori S, Seo T, Gudis K, et al. Diagnosis and treatment of obscure gastrointestinal bleeding using combined capsule endoscopy and double balloon endoscopy: 1-year follow-up study. Endoscopy 2007; 39:1053-8.
93. Li X, Dai J, Lu H, et al. A prospective study on evaluating the diagnostic yield of video capsule endoscopy followed by directed double-balloon enteroscopy in patients with obscure gastrointestinal bleeding. Dig Dis Sci 2009 August 12 [Epub ahead of print].
94. Marmo R, Rotondano G, Casetti T, et al. Degree of concordance between double-balloon enteroscopy and capsule endoscopy in obscure gastrointestinal bleeding: a multicenter study. Endoscopy 2009;41:587-92.
95. Koval G, Benner KG, Rsch J, et al. Aggressive angiographic diagnosis in acute lower gastrointestinal hemorrhage. Dig Dis Sci 1987;32:248-53.
96. Bloomfeld RS, Smith TP, Schneider AM, et al. Provocative angiography in patients with gastrointestinal hemorrhage of obscure origin. Am J Gastroenterol 2000;95:2807-12.
97. Berkelhammer C, Radvany A, Lin A, et al. Heparin provocation for endoscopic localization of recurrent obscure GI hemorrhage. Gastrointest Endosc 2000;52:555-6.
98. Mernagh JR, O'Donovan N, Somers S, et al. Use of heparin in the investigation of obscure gastrointestinal bleeding. Can Assoc Radiol J 2001; 52:232-5.
99. Askin MP, Lewis BS. Push enteroscopic cauterization: long-term follow-up of 83 patients with bleeding small intestinal angiodysplasia. Gastrointest Endosc 1996;43:580-3.
100. Morris AJ, Mokhashi M, Straiton M, et al. Push enteroscopy and heater probe therapy for small bowel bleeding. Gastrointest Endosc 1996;44: 394-7.
101. Barkin JS, Ross BS. Medical therapy for chronic gastrointestinal bleeding of obscure origin. Am J Gastroenterol 1998;93:1250-4.
102. van Cutsem E, Rutgeerts P, Vantrappen G. Treatment of bleeding gastrointestinal vascular malformations with oestrogen-progesterone. Lancet 1990;335:953-5.
103. Junquera F, Feu F, Papo M, et al. A multicenter, randomized, clinical trial of hormonal therapy in the prevention of rebleeding from gastrointestinal angiodysplasia. Gastroenterology 2001;121:1073-9.
104. Hodgson H. Hormonal therapy for gastrointestinal angiodysplasia. Lancet 2002;359:1630-1.
105. Rossini FP, Arrigoni A, Pennazio M. Octreotide in the treatment of bleeding due to angiodysplasia of the small intestine. Am J Gastroenterol 1993;88:1424-7.
106. Scaglione G, Pietrini L, Russo F, et al. Long-acting octreotide as rescue therapy in chronic bleeding from gastrointestinal angiodysplasia. Aliment Pharmacol Ther 2007;26:935-42.

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