

Evaluation & Management of Obscure Gastrointestinal Bleeding (OGIB)

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Summary:

Gastrointestinal bleeding is a common entity. Incidence of bleeding has comparatively increased though case fatality is static. Despite improved treatments and better understanding of the underlying pathophysiology of peptic ulcer disease the rising figures of GI bleeding reflect an increasing proportion of elderly population and non-steroidal anti-inflammatory use. Overall, 5% of all cases of gastrointestinal bleeding fall under the category of Obscure gastrointestinal bleeding (OGIB) in the USA. Obscure gastrointestinal bleeding is defined as bleeding of unknown origin that persists or recurs after an initial negative

endoscopic evaluation including colonoscopy and/or upper endoscopy. OGIB can be either Occult (no visible blood) or Overt (Passage of visible blood).

Less common aetiologies of GI bleeding e.g. Cameron erosions, Dieulafoy's lesion, Watermelon stomach that are sometimes difficult to identify at endoscopy often present as OGIB. They need special techniques even thrombolytic therapy to precipitate bleeding for diagnostic angiography. Increased awareness of the existence of such conditions help in rapid and accurate identification of the lesion. Review of such cases will be the focus of this publication.

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Introduction:

Bleeding from the upper gastrointestinal (GI) tract remains common, with a reported annual incidence of up to 172 per 100000¹, which has increased. Case fatality was recently reported as 14%² which is static, despite improved treatments and better understanding of the underlying pathophysiology of peptic ulcer disease. The rising figures may reflect an increasing proportion of elderly patients and non-steroidal anti-inflammatory use. Of patients in whom a diagnosis is confirmed, more than 90% suffer from peptic ulcers, oesophageal or gastric malignancy, varices, Mallory-Weiss syndrome, erosive disease and oesophagitis^{1,2}. Less common aetiologies of upper GI bleeding which are sometimes difficult to identify at endoscopy and manage will be the focus of this study.

Definition

Obscure gastrointestinal bleeding (OGIB) is defined as bleeding of unknown origin that persists or recurs after an initial negative endoscopic evaluation including

colonoscopy and/or upper endoscopy (esophagogastroduodenoscopy [EGD]).³ OGIB can be classified as either:

(1) Occult OGIB- which is manifested by recurrent iron deficiency anemia and/or recurrent positive fecal occult blood test (FOBT) results

(2) Overt OGIB- which is manifested as melena or hematochezia.

Overall, OGIB accounts for 5% of all cases of gastrointestinal bleeding in the USA⁴. Angiectasias of the small bowel are the most common source of OGIB and account for 30% to 40% of gastrointestinal bleeding in the elderly population, whereas tumors such as leiomyomas, carcinoids, lymphomas and adenocarcinomas are the predominant cause in patients aged 30 to 50 years⁵. Meckel's diverticulum, erosions and ulcers from nonsteroidal anti-inflammatory drug (NSAID) use⁶ and Crohn's disease of small bowel are also potential causes of OGIB. The term 'mid-gastrointestinal bleeding' rather than obscure bleeding is now applied if the origin is thought to be between papilla and ileocaecal valve⁷.

Causes of Obscure GI Blood Loss:

Common causes (any site):

Peptic ulcer, Reflux esophagitis, Erosive gastritis, Carcinoma (Specially colon), Vascular ectasia / angiodysplasia, Chron's disease

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Uncommon Causes (Upper GIT)

1. Esophagus / Stomach
Dieulafoy's lesion, Cameron's erosions with hiatal hernia, Prolapse erosions,
Gastric antral vascular ecstasia (Water melon stomach), Portal gastropathy, Varices
2. Small Intestine
Meckel's diverticulum, Celiac sprue, Chron's disease, Duodenitis

Uncommon Causes (Lower GIT)

3. Colon
Diverticula (obscure overt bleeding), Colitis (ulcerative/ ischaemic/ radiation injury), Endometriosis, Infection (hookworm, ascariasis, whipworm, strongiloidosis, amoebiasis, cytomegalovirus, tubercular entero colitis)
4. Rectum
Fissure, Haemorrhoid
5. Any site
Vasculitis, Telangiectasia, Aorto enteric fistula, Other cancers (lymphoma-gastric NHL, Kaposi's, leiomyoma, sarcoma, melanoma, carcinoids), Large polyps, Blue rubber bleb nevus syndrome, Haemangioma, Radiation damage, Amyloidosis
6. Extra intestinal
Haemobilia, Wirsungorrhoea, Haemoptysis, Epistaxis, bleeding gums
7. No source identified.

Angiodysplasia

Gastrointestinal angiodysplasias are the most common cause of obscure chronic blood loss from the digestive tract with small bowel angiodysplasia accounting for up to 40% of obscure GI bleeding⁸. The pathophysiology is unknown, but has been suggested to result from low grade venous obstruction of submucosal veins as they cross muscle layers^[9]. It is said to be more prevalent in chronic renal failure patients^[10] and in patients with aortic stenosis, although, recent reports have failed to confirm this link¹¹. Osler-Weber-Rendu Syndrome is an autosomal dominant condition characterized by angiodysplastic lesions involving the skin, mucosal membranes and organs other than the GI

tract (Figure 1). Their endoscopic appearance is indistinguishable from other angiodysplastic lesions (Figure 2) but more widespread.

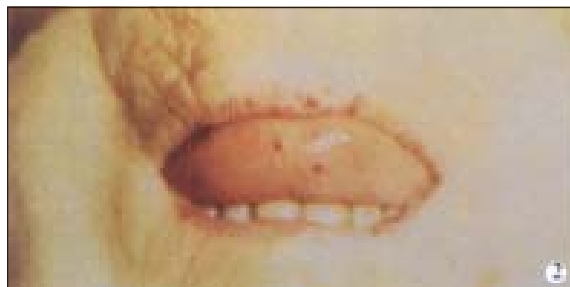


Fig.-1: Cutaneous manifest of O-W-R



Fig.-2: Mucosal lesion of OWR

Dieulafoy's Lesion

Dieulafoy's lesion is a cause of diagnostic difficulty in patients with repeated haematemesis. The exposed, eroded vessel in a very small mucosal defect is difficult to spot at endoscopy (Figure 3) and accounts for perhaps 2% of upper GI bleeds¹². It was described in detail by Dieulafoy¹³ in 1896 who termed 'Exulceratio Simplex' as bleeding from a simple tortuous aberrant submucosal artery of small size. The typical endoscopic appearance is that of a dark red 'nipple'.

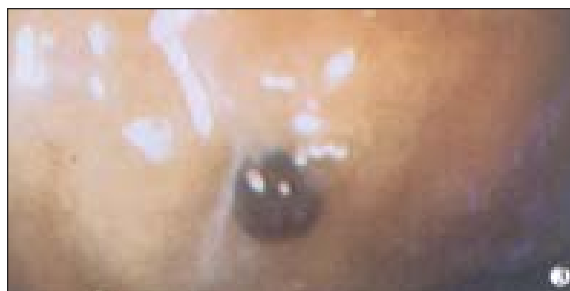


Fig.-3: Dieulafoy's lesion

Gastric Antral Vascular Ectasia (Watermelon Stomach)

This was first described in 1952 by Rider et al and used to be called gastric antral vascular ectasia. Jabbari et al [14] coined the phrase “watermelon stomach” to describe the endoscopic features (Figure 4). Recognition of this characteristic lesion is important since it is commonly dismissed by less experienced endoscopists as antral gastritis.

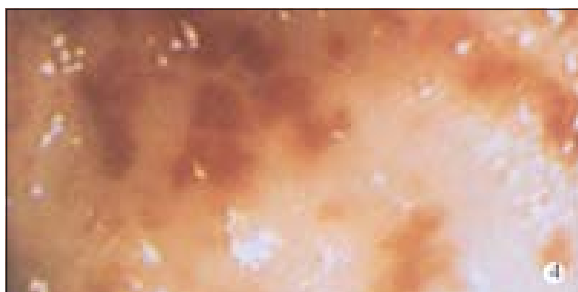


Fig.-4: *Watermelon stomach*

Cameron Erosions

Erosive disease is an uncommon cause of severe upper GI bleeding. However, some lesions warrant mentioning as they are often overlooked or missed at endoscopy. Cameron erosions are chronic linear erosions (Figure 5) positioned on the crests of folds at the diaphragmatic impression with a large hiatus hernia¹⁵.



Fig.-5: *Cameron lesion*

Prolapse Erosions

Prolapsing gastropathy is a focal area with subepithelial haemorrhage and occasionally, erosions within a few centimeters of the cardioesophageal junction. This mucosal area prolapses into the distal oesophagus commonly from 10 o'clock position during retching, often prior to haematemesis.

Unusual Upper GI Malignancies

Adenocarcinoma accounts for 90% of gastric tumours with lymphoma accounting for 5%, stromal tumours 2% and the rest include carcinoids, metastases and others. GI involvement occurs in 50% of non Hodgkins lymphoma, with the stomach being the most common extranodal site. 95% of gastric lymphomas are non-Hodgkins lymphoma.

Other Vascular Disorders

The Blue Rubber Bleb Naevus Syndrome (Figure 6) is an example of intestinal haemangioma which is an autosomal dominant condition causing GI bleeding in infants and children.



Fig.-6: *Jejunal phlebectasia*

Haemobilia

Bleeding from either the biliary tree (haemobilia) or from the pancreatic duct (Wirsungorrhagia) into the duodenum can be difficult to identify. Recent series indicate iatrogenic trauma accounting for 40% and accidental trauma 20%¹⁶. Classically, patients present with the triad of pain, jaundice and melaena. A history of chronic pancreatitis or pseudocyst may be a pointer to a bleed from the pancreatic duct.

Evaluation

Evaluation starts from elaborate history and careful bedside examination to provide clue to the cause of bleeding.

History

A history can reveal ingestion of medications known to cause bleeding (e.g., aspirin, nonsteroidal anti-inflammatory drugs, alendronate, potassium chloride, anticoagulants). A family history might suggest a hereditary vascular problem.

Physical Exam

The bedside examination may be helpful in providing clues to the cause of bleeding (Table I). Rare causes of bleeding may be detected on physical examination like Plummer-Vinson syndrome, acquired immunodeficiency syndrome (AIDS), neurofibromatosis, Osler-Weber-Rendu syndrome, pseudoxanthoma elasticum, amyloidosis (Figure 7) and other diseases with typical cutaneous manifestations¹⁷⁻¹⁸. Symptoms specific to the upper or lower intestinal tract may direct the initial endoscopic procedure, but data do not support limiting the evaluation to the symptomatic region.

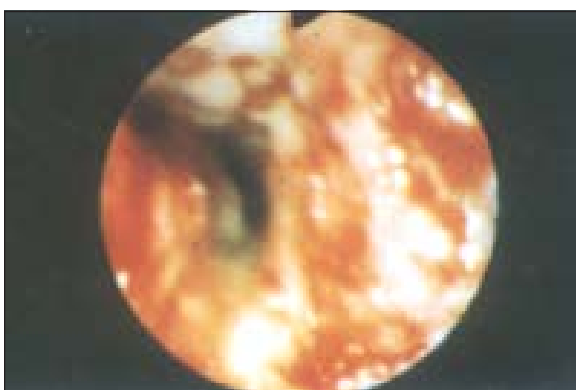


Fig.-7: *Intestinal amyloid*

Investigations

In OGIB, repeat EGD and colonoscopy with ileoscopy should be considered before performing a small bowel evaluation. A repeat EGD may yield a source even when the initial exam was negative. Zaman and colleagues reported that 64% of lesions identified with push enteroscopy were within reach of a standard endoscope¹⁹. Commonly missed lesions in the upper gastrointestinal tract include peptic ulcers, Cameron ulcers associated with large hiatal hernia, and angiectasias. Lesions often missed in the colon include angiectasias and neoplasms. The diagnostic yield of repeat EGD is sufficient to recommend a second-look endoscopy^{20,21,22}. Adequate inflation to distend the folds in the upper stomach, a retroflexed endoscope and close examination of the mucosa posteriorly on the lesser curve may help to identify Dieulafoy's. Multiple examinations are commonly required and the abnormality is sometimes diagnosed when pulsatile arterial bleeding is seen coming from apparently normal mucosa. In the absence of clear evidence of gastrointestinal bleeding, small-bowel biopsies should be taken to rule out celiac sprue in the evaluation of patients with iron deficiency anemia^{23,24,25}.

Gastrointestinal investigative techniques for occult and obscure bleeding are summarized in table II.

Table-I

Clinical Clues for Specific Causes of Gastrointestinal Bleeding

Age greater than 50	Carcinoma
Chronic renal failure	Vascular ectasia/angiodysplasia
Cutaneous hemangiomas	Blue rubber bleb nevus syndrome
Chronic diarrhea/abdominal pain	Celiac sprue
Acquired-immunodeficiency syndrome (AIDS)	Acquired-immunodeficiency syndrome (AIDS)

Table-II*Comparison of Gastrointestinal Investigative Techniques for Occult and Obscure Bleeding*

Method	Advantage	Disadvantage
Small bowel follow - through/enteroclysis	Minimal side effects or risk	Misses mucosal lesions Enteroclysis tube uncomfortable
Tagged red blood cell scan	Good for rapid bleeding of 0.1 -0.4 ml/min	Nonspecific, false localizations, and missed bleeding Cannot determine cause
Meckel's scan	Good in young patients to find diverticulum	Specific only for Meckel's diverticulum
Angiography	Good for rapid bleeding of >0.5 ml/min Can intervene in rapid bleeding if source is located	Invasive; risk of intestinal infarction with embolization Less likely to determine cause than endoscopy Risk of intravenous contrast reaction
Push enteroscopy	Direct visualization and intervention	Invasive, endoscopic risk, patient discomfort, misses part of jejunum and ileum
Capsule endoscopy	Allows examination of most of the small bowel Noninvasive	No intervention capability Physician interpretation is time-consuming
Method	Advantage	Disadvantage
Double balloon enteroscopy	Direct visualization and treatment of any part of small bowel lesion.	Invasive, endoscopic risk, patient discomfort, expensive, not widely available.
Single balloon enteroscopy	Rapid and easier to operate than double balloon	Not widely available
Endoscopic Ultrasound	Allows full thickness guided biopsy of abnormal mucosa	Not widely available
CT scan	Noninvasive	No intervention capability, expensive and low diagnostic yield

The British Society of Gastroenterology's guidelines propose small-bowel evaluation with capsule endoscopy as first test for patients with bleeding if no bleeding source is identified on upper and lower endoscopy, as diagnostic yield is highest during or soon after a bleeding

episode^{26,27}. On the basis of the findings, the clinician may proceed with push enteroscopy or double-balloon enteroscopy. Intraoperative enteroscopy should be reserved for patients with recurrent bleeding and transfusion dependency.

So in Patients with OGIB if endoscopic evaluation of upper and lower tracts is negative or equivocal, 2nd look examination by repeat upper and lower endoscopy is preferred before small bowel imaging [consensus/expert guidelines]. Cameron's erosions (within a hiatal hernia), peptic ulcer disease and vascular ectasias are the most common upper tract lesions found on repeat endoscopy, and cancer and angiodysplasias (Figure 8) are the most commonly overlooked lower tract abnormalities¹.



Fig.-8: *Bleeding jejunal ulcer*

Endoscopically lymphomas may present as enlarged gastric folds, mucosal nodularities, multiple polypoid masses with or without ulceration or with a diffuse infiltrative process. One unusual feature is that peristalsis is often preserved. Diagnosis can be difficult, sometimes requiring full thickness biopsy but when combined with endoscopic ultrasound (EUS) diagnostic accuracy approaches 100%.

Haemobilia or Wirsungorrhagia into the duodenum may require the use of a side viewing endoscope to make the diagnosis. It has been suggested that the endoscopic appearance at the ampulla of a filiform clot suggests biliary bleeding and of fresh bleeding a pancreatic origin. Angiographic or CT findings may be needed to make the diagnosis of an aneurysm, pseudoaneurysm or arterio portal venous fistula.

A history of abdominal aortic graft surgery should prompt a careful endoscopic examination of the second and third parts of the duodenum. If aorto-oesophageal fistula is suspected, CT investigation should be

undertaken prior to endoscopy in theatre since endoscopy can precipitate torrential bleeding.

Management

Importance of resuscitation can not be overemphasized. With adequate resuscitation as defined by hemodynamic stability there is significant reduction of post procedure complications. Antibiotic prophylaxis is another key component in the preparation prior to endoscopic intervention as there is likely development of transient bacteremia. Coagulation factor and platelet factor abnormalities should be assessed and corrected prior to endoscopy. Appropriate level of sedation can be reached through use of a benzodiazepine combined with a narcotic.

Endoscopy plays a major role in the evaluation of OGIB and the management approach is summarized in the flowchart (Table III).

Treatment and Outcome

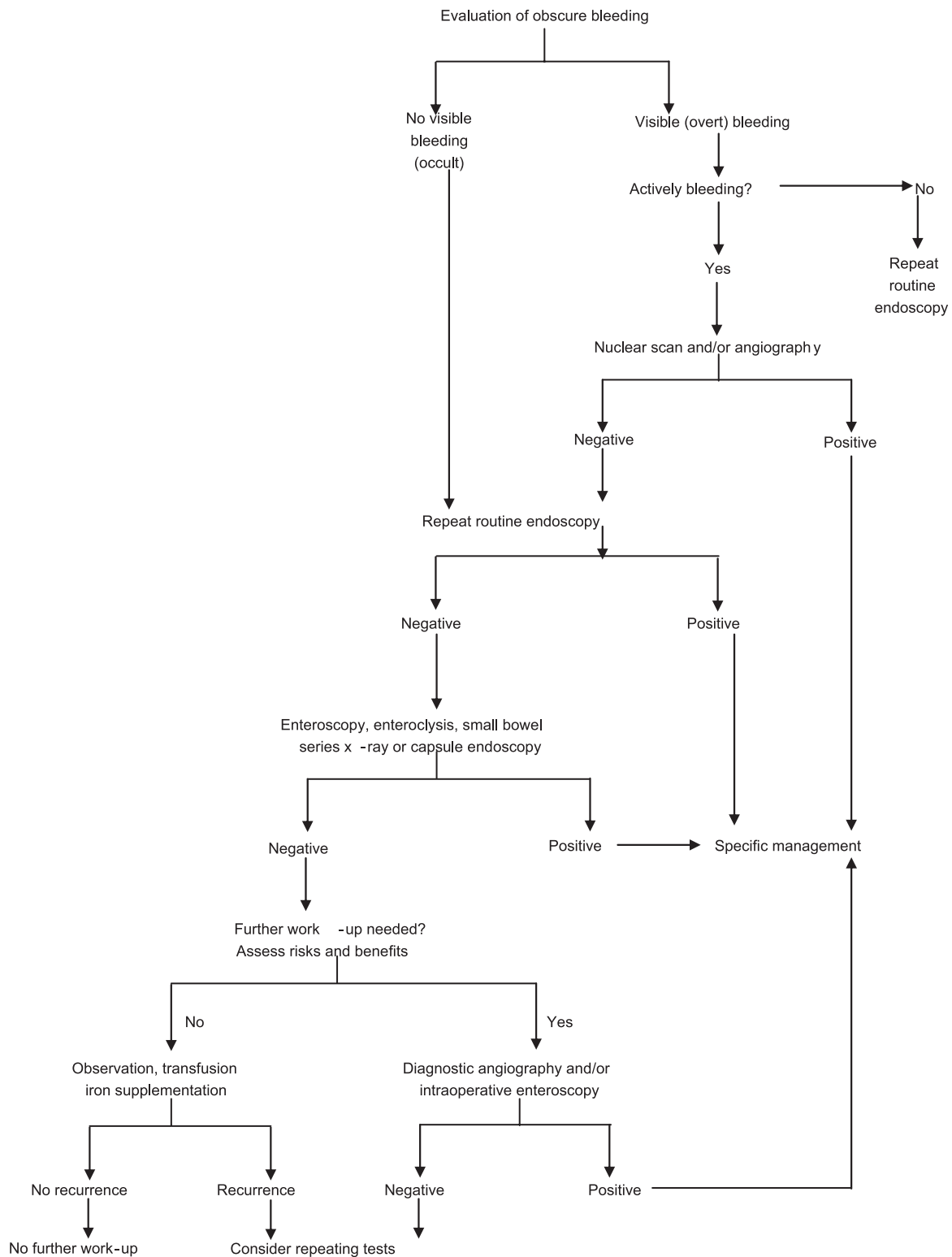
Treatment varies according to the etiology of bleeding, its severity and patient comorbidities. Treatment options include endoscopic, angiographic, pharmacotherapy, surgical therapies and non-specific measures. Endoscopic therapies include thermal contact probes, laser coagulation, injection sclerotherapy and banding.

Thermal ablation of bleeding is the treatment most commonly used for accessible lesions. Endoscopic therapy is successful in more than 90% of cases of Dieulafoy's bleeding. Adrenaline is frequently injected into the base prior to definitive treatment with electrocoagulation or more recently, band ligation. During angiography, interventional radiologists inject vasopressin or embolization material into bleeding vessels. Medical therapies are one of the few options available for diffuse vascular lesions, but they have limited success rates²⁸. Various thermal coagulation devices, including heater probes, bipolar probes, the Nd:YAG laser and the argon plasma coagulator appear to be successful in treating these lesions. Coagulation should begin at the central feeding arteriole and work peripherally. Primary treatment modality is the bipolar probe because it causes more superficial injury than other thermal methods. Laser treatment can cause deep injury relatively easily and must be used carefully.

Complication rates are low for gastric lesions and in the small bowel. Colonic complications are reported in

Table-III

Flowchart - Management plan of Obscure Bleeding



up to 10% cases and include partially treated lesions and perforation. Treatment is not required for incidental lesions. Treatment of isolated gastric lesions will often terminate bleeding, whereas many small bowel lesions are not reached and new lesions develop with time. Some patients will maintain a stable hemoglobin on iron therapy alone.

Gastrointestinal bleeding from arterial venous malformations has been successfully treated with combined hormone (ethinyl estradiol 0.035-0.05 mg; norethisterone 1 mg) therapy. However, continuous use of hormones for months has considerable side effects. The risk of thromboembolic events increases although observational studies have not confirmed a risk increase²⁹. With hereditary telangiectasias, von Willebrand's disease, or angiodysplasias in the setting of end-stage renal disease Octreotide (Sandostatin), given at a dosage of 0.05 to 0.1 mg subcutaneously two to three times per day, has been successful in case studies.

Treatment of lymphoma is according to histology and includes helicobacter eradication for MALT lymphomas.

Unless a single causative lesion is identified, surgical therapy should be a last resort. Currently, exploratory laparotomy is seldom preferred without concomitant intraoperative enteroscopy in cases of transfusion dependant bleeding³⁰. Patients with obscure bleeding often have multiple bleeding sites and bleeding may persist after surgery.

Non-specific therapy represents the primary approach to treatment in selected patients and should not be considered as failure of diagnostic approach. Non-specific measures include iron replacement, correction of coagulation or platelet disorders, intermittent blood transfusions if anemia cannot be corrected with iron supplement alone. These measures are beneficial when rate of blood loss is slow and in elderly patients in whom the risk of further diagnostic evaluation is greater.

Conclusion:

There is no single efficient diagnostic test or therapeutic approach in the management of obscure GI bleeding. Most patients will benefit from a meticulous investigative routine that attempts to visualize as much of the bowel as necessary. Definitive therapy may not be possible in all the cases.

Non specific measures are beneficial when rate of blood loss is slow and in the elderly. There have indeed been a number of improvements in the management of OGIB but morbidity is still high. Adopting new technologies (endoscopic ultrasound, confocal laser endomicroscopy, narrow band imaging and endoscopic suturing devices) may be helpful in conquering this challenging problem.

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