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Laparotomy and intraoperative enteroscopy for obscure gastrointestinal bleeding before and after the era of video capsule endoscopy and deep enteroscopy: a tertiary center experience

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Abstract

Background—To evaluate roles of intraoperative endoscopy (IOE) in management of severe obscure GI bleeding (OGIB) before vs. after introduction of video capsule endoscopy (VCE) and deep enteroscopy (DE).

Methods—We retrospectively reviewed prospectively collected data of patients undergoing IOE for severe OGIB in a tertiary referral center.

Results—52 patients had laparotomy/IOE for OGIB, 11 pre and 41 post VCE/DE eras. In the pre VCE/DE era, 36.4% (4/11) had preoperative presumptive diagnoses while in the post VCE/DE era presumptive diagnoses were made in 48.8% (20/41) (p= 0.18). Preoperative evaluation led to correct diagnoses in 18.2% (2/11) in the pre and 51.2% (21/41) in the post VCE/DE era (p=0.09). Vascular lesions and ulcers were the most common diagnoses, but rebleeding was common. No rebleeding was found among patients with tumors, Meckel's diverticulum, and aortoenteric fistula.

Conclusions—Presumptive diagnoses in the post VCE/DE era were usually accurate. If VCE or DE are negative, the probability of negative IOE is high. Patients with tumors and Meckel's diverticulum were the best candidates for IOE.

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Keywords

obscure gastrointestinal bleeding; deep enteroscopy; video capsule endoscopy; intraoperative enteroscopy; exploratory laparotomy

Introduction

Although obscure gastrointestinal bleeding (OGIB) accounts for only about 5% of gastrointestinal hemorrhage, it is a clinically significant and potentially expensive medical problem that often results in multiple blood transfusions, frequent hospitalizations, and repetitive diagnostic evaluations.[1]

In the past, the standard evaluation for patients with OGIB was limited to esophagoduodenoscopy (EGD), push enteroscopy, colonoscopy, and radiologic studies of the small bowel (e.g. tagged RBC scan, technetium-99m scan, angiography, and small bowel computerized tomography [CT]). However, these tests are unable to completely examine the small bowel despite 75% of OGIB cases originating from the small bowel.[2–4] Moreover, even with standard push enteroscopy, only 50 to 100 cm of small bowel can be visualized beyond ligament of Treitz.[4] Therefore, in the past intraoperative enteroscopy (IOE) was required for complete small bowel evaluation and treatment in patients with severe recurrent OGIB. [5-8]

Since their introduction, video capsule endoscopy (VCE) and deep enteroscopy (DE) have proven to be superior to other conventional tests for diagnosis of OGIB.[9-133] Additionally, simultaneous tissue diagnosis by biopsies and treatment can be delivered during DE. These advances have resulted in more accurate diagnosis and significant improvement in the management of patients with OGIB.

We aim to evaluate the roles of intraoperative endoscopy (IOE) in management of severe obscure GI bleeding (OGIB) in the eras before and after the introduction of VCE/DE. We compared the outcomes such as rebleeding in the two eras. Our hypothesis was that with the introduction of VCE/DE, accurate preoperative diagnosis could be achieved more frequently than before and clinical outcomes would improve after surgery.

Material and Methods

We retrospectively analyzed prospectively collected data of patients diagnosed with severe OGIB undergoing exploratory laparotomy with or without IOE at Ronald Reagan UCLA Medical Center from 1990 to 2013. The study protocol was approved by the hospital Institutional Review Board (IRB). We utilized a 2007 American Gastroenterology Association (AGA) management guideline that defined OGIB as persistent gastrointestinal bleeding with no obvious etiology after EGD, colonoscopy, and other radiologic evaluations.[14] OGIB was further subdivided into overt OGIB and occult OGIB according to the presence or absence of visible blood in the stool or melena. Baseline characteristics including age, gender, ethnicity, co-morbidities, baseline laboratory results (e.g. initial hemoglobin, platelet, international normalized ratio = INR), medications, the American Society of

Anesthesiologists (ASA) classification, and quantity of blood transfusions during the same admission of the surgery were also recorded. Center for Ulcer Research and Education (CURE) prognostic scores were calculated for each patient.[15] At our institution, VCE and DE were introduced in 2001. Therefore, study patients were categorized into pre VCE/DE era group if they were evaluated for IOE before 2001 and as post VCE/DE era group if they were evaluated in or after 2001. In order to reduce discrepancies in classification of arteriovenous malformations (AVM), angiodysplasia, and vascular ectasia, these diagnoses were labeled as "vascular lesions." This diagnosis excluded small bowel varices.

Preoperative diagnoses

Findings from EGD, colonoscopy, push enteroscopy, radiologic evaluations, double balloon enteroscopy (DBE), single balloon enteroscopy (SBE), and spiral enteroscopy (SE) of all patients were recorded. The preoperative findings were reviewed and subsequently categorized into three groups according to the strength of evidence for preoperative diagnosis. If no specific lesion was found as the source of bleeding, they were classified as "non-diagnostic". If preoperative tests provided localization of the bleeding site without identifying a lesion, the results were classified as "localization" but not etiologic. Finally, lesions which were thought to be causative based upon location, stigmata of hemorrhage, and clinical evidence were classified as "presumptive diagnosis".

Operative and IOE diagnoses

During the laparotomy, the stomach, small bowel, colon, and mesentery were mobilized, inspected, and palpated for transmural, serosal, or mass lesions. If no culprit lesion was found, an IOE was then collaboratively performed by the gastroenterologist and surgeons. Based upon the preoperative localization of the bleeding site and the presumptive diagnosis, the entry site of IOE was determined. Per-oral, enterotomy, or per-anal enteroscopies were performed when proximal, middle, or distal part of small bowel were the suspected locations respectively and no lesion was found on inspection at laparotomy. Transillumination was also utilized to assist identification of vascular and other lesions. Inspection of the gastrointestinal mucosa and lumen with IOE was primarily done during advancement of the enteroscope to minimize false positive results from trauma during small bowel manipulation and withdrawal.

A definitive diagnosis was made during IOE when lesions were identified with active bleeding or other major stigmata of recent hemorrhage (e.g. visible vessel or adherent clot). An ulcer in the diverticulum upon opening it and confirmed by surgical pathology was classified as a Meckel's diverticulum hemorrhage. The diagnosis of "vascular lesions" including angiodysplasia, arteriovenous malformations or angiomas was made by visual inspection without biopsies. Furthermore, we diagnosed patients with vascular lesions as the cause of OGIB when 1) active bleeding was present during IOE from or near the lesions, in the absence of other findings, 2) multiple or extensive lesions were found in the absence of other gastrointestinal lesions, 3) a vascular lesion was found on IOE at the same location identified by preoperative evaluation, such as capsule endoscopy, and/or 4) a large lesion (e.g. > 5-10 mm) was found with a visible vessel or adherent clot or spontaneous bleeding with mild water jet irrigation.

Follow-up and Rebleeding

Follow up information was obtained from prospectively collected data from the CURE: Digestive Diseases Research Center (DDRC) database. Rebleeding was defined as: 1) recurrence of hematochezia or melena, or 2) recurrence of iron deficiency anemia, with fecal occult positive stools, with 3) a decrease in hemoglobin from baseline of ≥ 2 grams and/or RBC transfusion of 1 or more units of blood and overt bleeding or fecal occult positive blood tests. Significant complications and postoperative adverse events including those related to the operation or co-morbidities were assessed.

Data and Statistical analyses

Demographic and laboratory characteristics, diagnostic yield, number of patients with preoperative presumptive diagnosis and/or localization, and final diagnoses were compared between the pre and post VCE/DE eras. The rebleeding rates for patients with vascular lesions or no diagnosis were also compared to patients with other diagnoses.

Statistic Package for the Social Sciences version 22.0 was utilized for statistical analysis. All numerical data were expressed as means and ranges. Frequencies were presented as numbers of patients and percentages. Continuous variables were compared using the student's t-test or analysis of variance. Fisher exact tests and Pearson Chi-square tests were used to compare nominal variables between the two groups (pre and post VCE/DE eras) and other categorical variables. P-values less than 0.05 were considered significant.

Results

52 patients underwent laparotomy and/or IOE for evaluation and treatment of recurrent severe OGIB during the study period. Eleven patients were in the pre and 41 patients in the post VCE/DE eras. Figure 1 shows a flowchart of all patients according to their preoperative presumptive diagnoses and localization of bleeding and their diagnostic yield of laparotomy and IOE. Demographic and baseline characteristic of both groups are shown in Table 1. The majority of patients had overt OGIB in both eras (81.8% in the pre and 92.7% in the post VCE/DE era). Patients who underwent laparotomy and/or IOE in the post VCE/DE era received significantly more PRBC transfusions during the same admission compared with the pre VCE/DE era (8.6±8.7 vs 4.4±1.5 units, p= 0.02).

Preoperative and IOE diagnoses

In the pre VCE/DE era, four patients (36.4%) had presumptive diagnoses prior to the operation while in the post VCE/DE era presumptive diagnoses were found in 20 patients (48.8%) (p= 0.18) (Figure 1). In the pre VCE/DE era, 2 patients (50%) with presumptive diagnoses had diagnoses confirmed intraoperatively, including 1 with vascular lesions and 1 with a small bowel tumor. For the other 2 patients with preoperative presumptive diagnoses of vascular lesions, in addition to vascular lesions 1 was found intraoperatively to have a small bowel tumor and 1 was found to have a small bowel ulcer. In the post VCE/DE era, 16 patients with preoperative presumptive diagnoses had the diagnoses confirmed intraoperatively, including 7 small bowel ulcers, 5 vascular lesions, 1 small bowel tumor, 1 Meckel's diverticulum, 1 aortoenteric fistula, and 1 small bowel varices. For the other 4

patients with presumptive diagnoses, 2 with presumptive diagnoses of vascular lesions and 1 with small bowel ulcer did not have these confirmed intraoperatively and 1 other patient with a presumptive diagnosis of vascular lesions was found to have a small bowel tumor diagnosed during laparotomy.

Among the six patients with preoperative localization of bleeding in the post VCE/DE era, 5 patients had causative lesions in the same location (3 vascular lesions, 1 small bowel ulcer, and 1 Meckel's diverticulum), while one other patient had no lesion found intraoperatively. All 7 patients in the pre VCE/DE era without either a presumptive diagnosis nor localization of bleeding were found intraoperatively to have causative lesions. These included 2 small bowel tumors, 1 with vascular lesions, 1 small bowel ulcers, 1 Meckel's diverticulum, 1 focal Crohn's disease, and 1 with terminal ileal ischemia. In the post VCE/DE era, among the 15 patients without either presumptive diagnoses or localization, 9 (60%) were found intraoperatively to have causative lesions, including 2 vascular lesions, 3 small bowel tumors, 2 small bowel ulcers, 1 Crohn's disease, and 1 aortoenteric fistula. The other 6 patients (40%) without a presumptive diagnoses or localization had negative IOE.

Preoperative evaluation led to correct diagnoses in 2 patients (18.2%) in the pre and 21 patients (51.2%) in the post VCE/DE era (p=0.09). The rates of diagnosis confirmation or finding another diagnosis at laparotomy and/or IOE for patients with preoperative presumptive diagnoses of both eras are shown in figure 2 and these results are also shown in patients without presumptive diagnoses or localization of bleeding in Figure 3.

Definitive diagnoses

A total of 43 patients had definitive diagnoses found intraoperatively with or without IOE, including 11 patients in the pre and 32 patients in the post VCE/DE era. In the pre VCE/DE era, 100% (11/11) of patients had definitive diagnoses made intraoperatively, whereas in the post VCE/DE era 75.6% of patients (31/41) had definitive diagnoses found intraoperatively. (Table 2) In the post VCE/DE era, one other patient had active bleeding from vascular lesions diagnosed with VCE, but this was not confirmed by IOE. The three most common definitive diagnoses were small bowel vascular lesions, ulcers, and tumors which were responsible for 79.1% (34/43) of all diagnoses. In the post VCE/DE era, preoperative evaluation led to definitive diagnoses in 81.8% (9/11) of vascular lesions, 70% (7/10) of ulcers, and 40% (2/5) of small bowel tumors (Figure 4).

In the pre VCE/DE era, locations of definitive diagnoses were 2 in the duodenum, 2 in jejunum, 4 in ileum, and 2 at small bowel anastomoses. In the post VCE/DE era, locations of definitive diagnoses were 2 in duodenum, 6 in jejunum, 9 in ileum, 2 at small bowel surgical anastomoses, 12 in an unspecified part of the small bowel, and 1 with diffuse lesions in the small bowel. No gastric or colonic lesions were diagnosed as the cause of severe OGIB in these patients.

Rebleeding rate

Forty-one patients had follow up information including 10 patients in the pre and 31 patients in the post VCE/DE era. The follow-up duration in the pre VCE/DE was 450 ± 872 days and in the post VCE/DE was 324 ± 481 days. Rebleeding rates of each diagnoses in both eras are

shown in Table 3. For lesions that were surgically resectable, no postoperative bleeding occurred. These included small bowel tumors, Meckel's diverticulum, aortoenteric fistula, and focal ischemia. However, rebleeding developed in 66.7% (8/12) of patients with vascular lesions, 44.4% (4/9) of patients with small bowel ulcers and 50% (1/2) of patients with Crohn's disease. In patients with no definite diagnosis, 62.5% (5/8) developed rebleeding.

Morbidity and mortality

The overall adverse event rate was 63.6% (7/11) in the pre and 43.9% (18/41) in the post VCE/DE (p=0.32). All adverse events were post-operative and the majority (69%) (20/29) were related to cardiopulmonary diseases in 10 patients, infections in 3, gastrointestinal bleeding in 2, and other non-surgical complications in 5. Postoperative complications related to the operation accounted 31% of adverse events (9/29). These were seen in 5 patients with surgical leaks or fistulas and 4 patients with postoperative ileus for greater than 4 days. Thirty-day mortality was 18.2% (2/11) in the pre VCE/DE era and 4.9% (2/41) post VCE/DE era (p= 0.19).

Discussion

Although this study was relatively small and underpowered, we found several important clinically relevant observations about the role of IOE in the management of severe OGIB in the post VCE/DE era. Patients undergoing laparotomy and/or IOE in the post VCE/DE era received significantly more RBC transfusions during the same admission prior to the operation than in the pre VCE/DE era (8.6±8.7 units, 4.4±1.5 vs. p= 0.02). This probably related to more new tests performed pre-operatively in the post VCE/DE era. Presumptive diagnoses or localization in the post was higher than the pre VCE/DE era, although this was not significant (63.4% vs 36.4%, p=0.18). Presumptive diagnoses or localization led to correct diagnoses in 51.2% in the post compared with 18.2% in the pre VCE/DE (p=0.09). Most important clinically, 80% of patients with preoperative presumptive diagnoses were confirmed by laparotomy and/or IOE in the post compared with 50% in the pre VCE/DE era (p = 0.25). In contrast, patients with negative preoperative presumptive diagnoses or localization in the post VCE/DE era had negative findings during the operation in 40% compared with 0% in the pre VCE/DE era. Rebleeding was not found in any patients with focal surgically resectable lesions (Meckel's diverticulum, small bowel tumors, focal ischemia, or aortoenteric fistulae) whereas rebleeding occurred commonly in multiple lesions, including 66.7% of patients with vascular lesions, 44.4% of small bowel ulcers, and 62.5% of patients with negative IOE.

Based upon our results, we developed an algorithm for diagnosis and treatment of severe obscure GI hemorrhage that is overt in the current era. Refer to Figure 5. Prior to surgery, making a presumptive diagnosis and excluding vascular lesions or other diffuse (non-focal) lesions as the source, and/or localizing the bleeding site should improve the yield of laparotomy and intraoperative enteroscopy in the current era.

Severe OGIB has always been a challenging gastrointestinal problem. Since the development of VCE and DE, several studies have reported the superiority of VCE and DE compared to radiographic evaluation or push enteroscopy. However, impact of VCE and DE

on laparotomy and IOE for OGIB has never been reported. [9-13] In our study, 63.4% of patients in the post VCE/DE era were found to have a preoperative presumptive diagnoses or localization of the bleeding site. This finding is consistent with other published data. In a meta-analysis evaluating the role of VCE and DE in the setting of OGIB, the overall diagnostic yield of VCE was 60% while the diagnostic yield of DE was 57%.[16] Additionally, 80% of patients with preoperative presumptive diagnoses had the same lesions confirmed during the operation. This finding is also similar to a study by Douard et al which reported that 13 of 15 patients (80%) with positive VCE preoperatively had the same diagnoses confirmed during IOE.[17] Hartmann also found that IOE confirmed diagnoses in 95% of patients with a positive VCE.[18] Diagnostic yield of DBE for patients with OGIB also appeared similar.[12,19,20] When DBE was performed prior to IOE, 95% of lesions diagnosed by DBE were confirmed by IOE.[11] These findings emphasize that VCE and DE have an important role and are highly accurate for diagnosis and localization of lesions in patients with severe OGIB prior to laparotomy and/or IOE. As a result, VCE and DE should be performed in patients with severe or recurrent OGIB prior to laparotomy or IOE, as shown in Figure 5.

The decision to proceed with IOE when VCE and/or DE are negative is controversial. In this study 60% of patients with negative preoperative evaluation in the post VCE/DE ultimately were found to have causative lesions during IOE. Similarly, a study by Douard et al reported that 66.7% (2/3) patients with negative VCE ultimately had a diagnosis made during IOE.[17] In contrast, Hartmann reported that only 14.2% (1/7) of patients with negative VCE were found to have a lesion diagnosed at IOE.[18] Therefore, gastroenterologists and surgeons should be more careful in selecting patients for IOE when VCE and/or DE are negative. However, when significant rebleeding occurs, it is reasonable to repeat VCE and DE until either localization or lesions are found, before proceeding with laparotomy and IOE, as shown in Figure 5.

Other important factors should be considered before proceeding with IOE include assessment of the benefits and risk of rebleeding and the risk of complications from the operation. In our study, patients with surgically resectable lesions benefited the most. No rebleeding occurred in patients with small bowel tumors, Meckel's diverticulum, focal ischemia or aortoenteric fistulae. In contrast, patients with small bowel angiomas, multiple ulcers, and patients with negative IOE often rebleed (66.7%, 44.4%, and 62.5% respectively). Rebleeding rates of vascular lesions are known to be as high 52%.[21] However, rebleeding rates of patients with ulcers or negative IOE are not often reported.[21] Kendrick et al reported that 14 patients with negative IOE had a rebleeding rate of 57% (8/14), while Douard et al found that the rebleeding rate of patients with negative IOE was 30% (6/20). [22,23] Therefore, these data call into question whether IOE should be performed in patients with negative VCE and/or DE considering the low yield of IOE and high rebleeding rate.

Lastly, the morbidity and mortality of patients after IOE should be considered. In our study, the overall morbidity rates were 63.6% in the pre and 43.9% in the post VCE/DE era, whereas, the overall mortality rates were 18.2% in the pre and 4.9% in the post VCE/DE eras. Although the differences were not significant, the arithmetic decreases in morbidity and mortality after IOE are clinically important. In another report, morbidity rates were

reported to be 12.5% to 50% between 1989 to 1999 and 1.2% to 33.3% between 2000 to 2009 while mortality rates were 0% to 17.6% between 1989 to 1999 and 0% to 11.1% between 2000 to 2009.[21] Improvements in critical care management, endoscopic advancements, surgical expertise and surgical techniques probably all contribute to these decreases in morbidity and mortality.

There are limitations in our study. First, the sample size of the study was relatively small, especially in the pre VCE/DE era, which contributed to inadequate power to show statistical differences. Second, the retrospective nature of the study along with differences over time in management of patients could have affected outcomes. Nevertheless, our study demonstrated several important observations about the role of VCE and DE prior to IOE.

Conclusions

In conclusion, we recommend IOE for patients with severe OGIB when VCE or DE is positive and endoscopic treatment cannot be performed by DE. If VCE and/or DE are negative, VCE, DE, or other tests should be repeated when severe rebleeding occurs to identify a lesion or location, considering the reported low yield of IOE (Figure 5). Patients with surgically treatable conditions such as small bowel tumors, aortoenteric fistulae, focal ischemia and Meckel's diverticulum had the best outcomes and therefore are the best candidate for IOE when they have presumptive diagnoses. In contrast, rebleeding rates of patients with negative IOE or vascular lesions were high. Therefore, gastroenterologists and surgeons should be very cautious about recommending laparotomy and IOE for patients with negative preoperative evaluations or vascular lesions in the era of VCE/DE.

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Table of Abbreviations Used

AGA	American Gastroenterology Association
ASA	American Society of Anesthesiologists
AVM	arteriovenous malformation
CT	Computerized tomography

CURE	DDRC, Center for Ulcer Research and Education: Digestive Diseases Research Center
DBE	Double balloon enteroscopy
DE	Deep enteroscopy
EGD	Esophagogastroduo denoscopy
GI	Gastrointestinal
GISTS	Gastrointestinal stromal tumors
INR	International normalized ratio
IOE	Intraoperative enteroscopy
MRI	Magnetic resonance imaging
NSAIDS	non-steroidal anti-inflammatory drugs
PRBC	Packed red blood cell
SBE	Single balloon enteroscopy
SE	Spiral endoscopy
VCE	Video capsule endoscopy

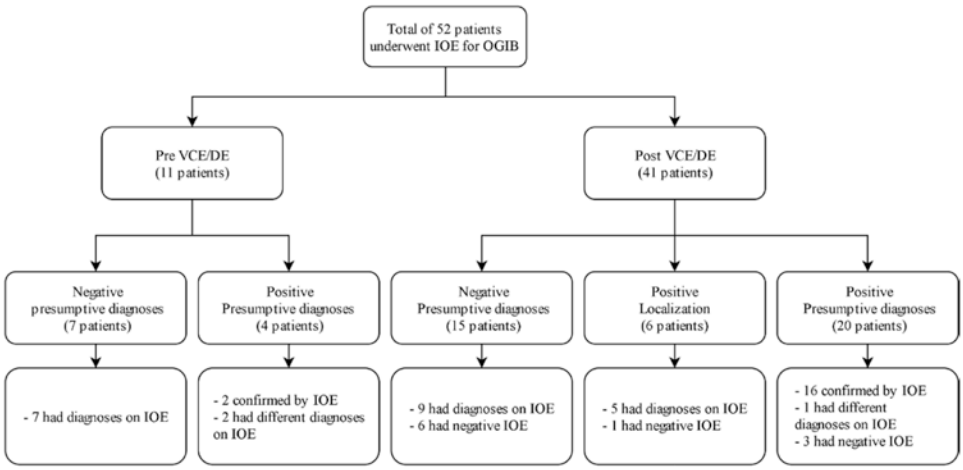

Figure 1. Flowchart showing diagnostic yield in the pre and post VCE/DE eras according to preoperative findings

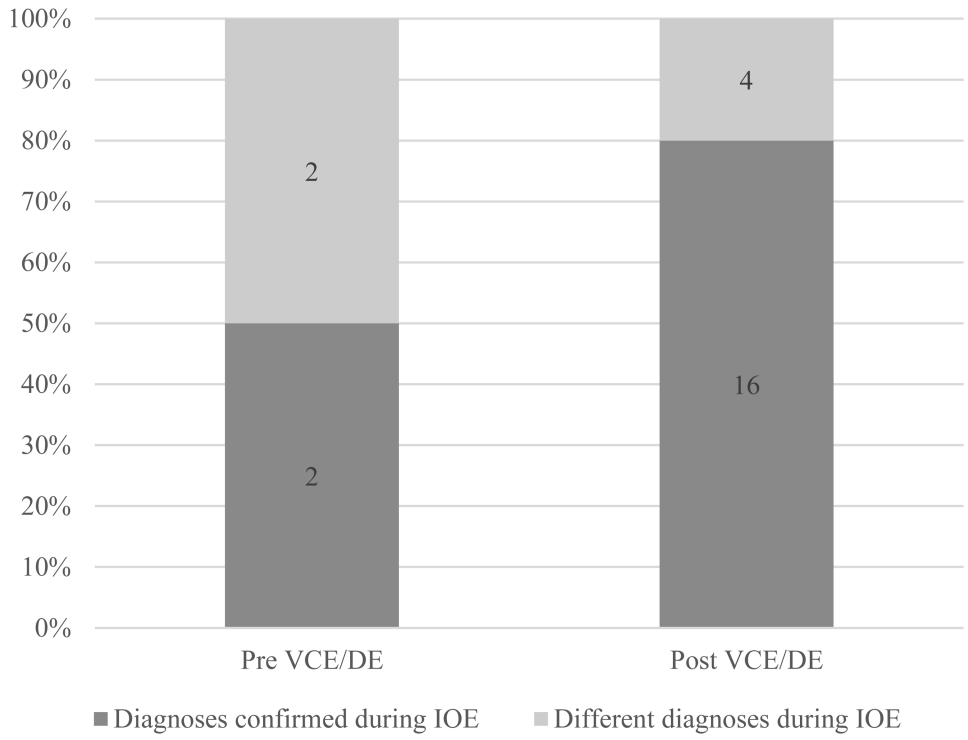

Figure 2. Confirmation of preoperative diagnosis or finding a different diagnosis at laparotomy and/or IOE. (p=0.25)

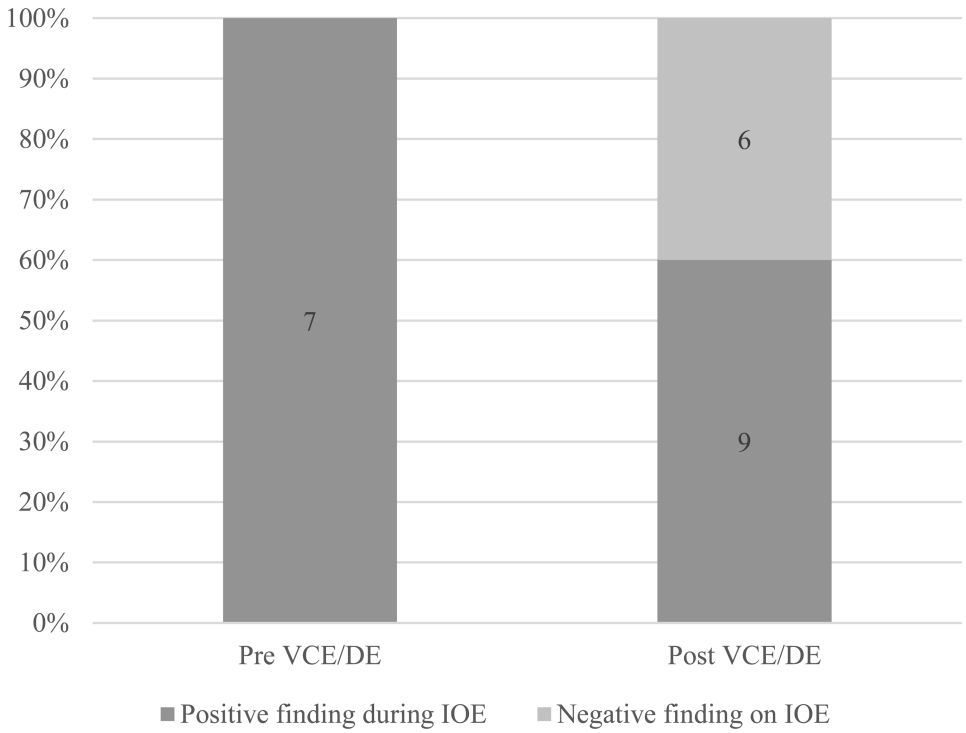

Figure 3. Diagnostic yield of laparotomy and/or IOE for patients with no preoperative presumptive diagnoses nor localization by pre and post VCE/DE eras. (p=0.12)

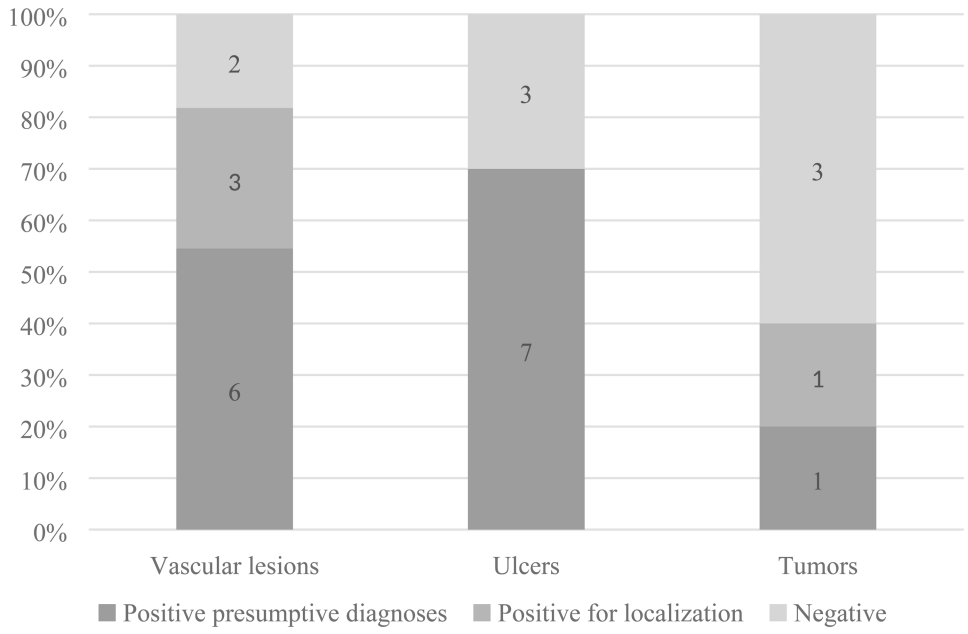

Figure 4.
Results of preoperative presumptive diagnoses and localization of bleeding for the three most common diagnoses in the post VCE/DE era.

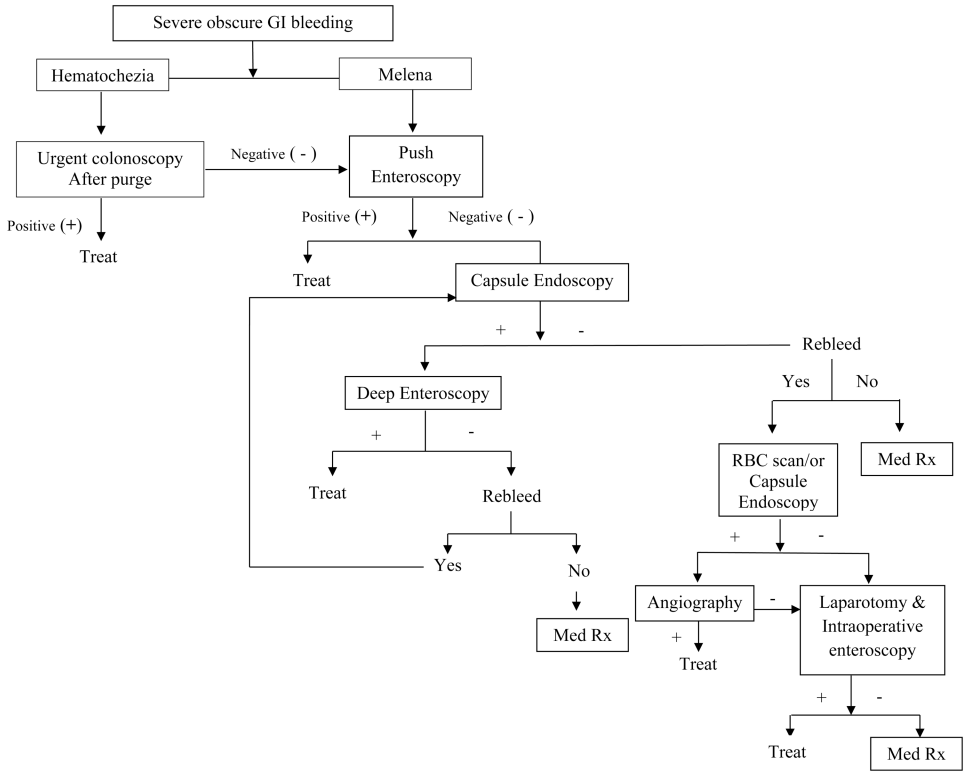

Figure 5. CURE Hemostasis Unit Algorithm for Severe Obscure GI Bleeding

Table 1

Demographic and baseline characteristic of patients in the pre and post VCE/DE

	Pre VCE/DE N=11	Post VCE/DE N= 41	P value
Age, years	57.73±17	55.9±17	0.77
Male gender, % (n)	54.5% (6/11)	65.9% (27/41)	0.50
Overt OGIB, % (n)	81.8% (9/11)	92.7% (38/41)	0.28
Occult OGIB, % (n)	18.2 (2/11)	7.3% (3/41)	
Total units of PRBC transfusion	4.4±1.5	8.6±8.7	0.02
Follow up duration - days (not baseline data – Move)	450±872	324±481	0.69
Hgb (g/dL)	9.2±1.2	9.5±2.5	0.68
Aspirin, % (n)	9.1% (1/11)	5.1% (2/41)	0.52 *
NSAIDs, % (n)	0% (0/11)	0% (0/41)	-
Anticoagulants, % (n)	0% (0/11)	5.1% (2/41)	-
ASA Classification	2.6±0.7	2.6±0.8	0.94
CURE Prognostic Scores	1.9±1.0	2.2±1.2	0.49

OGIB is obscure gastrointestinal bleeding; PRBC is packed red blood cell; Hgb is hemoglobin (when hospitalized, before transfusion); NSAID's are non-steroidal anti-inflammatory drugs; ASA is American Society of Anesthesiologists; CURE is Center for Ulcer Research and Education.

* Fisher's Exact Test

Table 2

The definitive diagnosis for severe OGIB in the eras before vs. after VCE and DE.

Type of lesions	Pre VCE/DE	Post VCE/DE	Total
1. Small bowel vascular lesions	2	11	13 (30.2%)
2. Small bowel ulcers	2	10	12 [*] (27.9%)
3. Small bowel tumors	4	5	9 [†] (20.9%)
4. Meckel's diverticulum	1	2	3 (7%)
5. Aortoenteric fistula	0	2	2 (4.7%)
6. Focal Crohn's disease	1	1	2 (4.7%)
7. Small bowel varices	0	1	1 (2.3%)
8. Terminal ileum ischemia	1	0	1 (2.3%)

[*] 5 anastomotic ulcers and 7 small bowel ulcers.

[†] 5 Gastrointestinal stromal tumors (GISTs) and 4 adenomas.

Table 3

Rebleeding rates of patients with each diagnosis in 41 patients with follow-up.

	Pre VCE/DE	Post VCE/DE	Total
Vascular lesions	50% (1/2)	70% (7/10)	66.7% (8/12)
Small bowel ulcers	50% (1/2)	42.56% (3/7)	44.4% (4/9)
Small bowel tumor	0% (0/3)	0% (0/3)	0% (0/6)
Meckel's diverticulum	0% (0/1)	0% (0/1)	0% (0/2)
Crohn's disease	0% (0/1)	100% (1/1)	50% (1/2)
Aortoenteric fistula	n/a (0/0)	0% (0/1)	0% (0/1)
Ischemia	0% (0/1)	n/a (0/0)	0% (0/1)
No definite diagnosis	n/a (0/0)	62.5% (5/8)	62.5% (5/8)
Total	20% (2/10)	51.6% (16/31)	43.9% (18/41)