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ORIGINAL ARTICLE

Early intervention with double balloon enteroscopy for higher yield for inpatient overt obscure gastrointestinal bleeding: A propensity matched analysis

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bleed, double balloon enteroscopy, gastrointestinal, obscure, overt.

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Abstract

Background and Aim: Overt obscure gastrointestinal bleeding (OOGIB) is defined as continued bleeding with unknown source despite esophagogastroduodenoscopy (EGD) and colonoscopy evaluation. Small bowel evaluation through video capsule endoscopy (VCE) or double balloon enteroscopy (DBE) is often warranted. We studied the timing of DBE in hospitalized OOGIB patients regarding diagnostic yield, therapeutic yield, and GI rebleeding.
Methods: We performed a retrospective review of DBEs performed at a tertiary medical center between November 2012 and December 2020. The inclusion criterion was first admission for OOGIB undergoing DBE. Those without previous EGD or colonoscopy were excluded. Patients were stratified into two groups: DBE performed within 72 h of OOGIB (emergent) and beyond 72 h of OOGIB (nonemergent). Propensity score matching was used to adjust for the difference in patients in the two groups. Logistic regression analysis was used to assess factors associated with diagnostic and therapeutic yield. Kaplan–Meir survival curve showed GI bleed-free survival following initial bleed and was compared using the log rank test.
Results: A total of 154 patients met the inclusion criterion, of which 62 had emergent DBE and 92 had nonemergent DBE. The propensity-score-matched sample consisted of 112 patients, with 56 patients each in the emergent and nonemergent groups. Univariate and multivariable logistic regression analysis showed a significant association between VCE and emergent DBE and diagnostic and therapeutic yield ($P < 0.05$). Emergent DBE patients had increased GI bleed-free survival compared to those in the nonemergent group ($P = 0.009$).
Conclusion: Our data demonstrate that emergent DBE during inpatient OOGIB can impact the overall diagnostic yield, therapeutic yield, and GI rebleeding post DBE.

Introduction

Obscure gastrointestinal (GI) bleeding is defined as bleeding with unknown source despite esophagogastroduodenoscopy (EGD) and colonoscopy evaluation. This accounts for up to 5–10% of GI bleeding.[1,2] When patients continue to present with evidence of active bleeding either in the form of hematochezia or melena after negative upper and lower endoscopic investigation, their bleed is classified as overt obscure gastrointestinal bleeding (OOGIB).[3] More recently, there has been a shift in terminology for "obscure GI bleeding" with "small bowel bleeding" or "suspected small bowel bleeding," but OOGIB is still used in general practice.[4]

OOGIB is often suspected to originate in the small bowel, with common culprit lesions consisting of Dieulafoy's lesions, neoplasias, angioectasias/angiodysplasias, ulceration, and polyps.[1,5,6] Although the phrase "arteriovenous malformations" (AVMs) is still used by clinicians, American College of Gastroenterology (ACG) guidelines have replaced this phrase with "gastrointestinal angiodysplasia."[1] Diagnostic approaches in situations of OOGIB include video capsule endoscopy (VCE),[7] radiographic imaging in the form of computed tomography (CT) scans,[8] push enteroscopy,[9] or deeper endoscopic procedures including balloon enteroscopy.[10] The European Society of Gastrointestinal Endoscopy (ESGE) has recommended that in instances of obscure GI bleeding, VCE be

implemented as the first-line diagnostic modality; however, in instances of OOGIB, they recommend VCE as soon as possible (ideally within 14 days) to maximize the overall diagnostic yield. Any lesions identified on VCE should then be confirmed and potentially treated with device-assisted enteroscopy.[11,12]

The importance of identifying and treating small bowel lesions leading to OOGIB is represented in the overall rebleeding risk. Literature shows that the rebleeding rate in untreated lesions found on VCE to be as high as 40%.[13–15] Even after direct endoscopy-guided therapy, rebleeding rates have still been reported to be as high as 9%.[14,16] Given the high rebleed risk, modalities tailored to increase diagnostic yield are increasingly important for long-term outcomes of these patients.[5,10,17]

Timing of device-assisted enteroscopy from the onset of initial bleed for OOGIB has been discussed, with most data demonstrating the benefits of performing the procedure as soon as possible to increase the overall diagnostic and therapeutic yield.[18–20] During inpatient admissions, prompt timing of DBE can be quite challenging, given the myriad hospital parameters and patient factors. We aimed to assess whether the timing of DBE for OOGIB in the inpatient setting had impacts on overall diagnostic and therapeutic yields as well as on GI rebleeding post DBE.

Methods

Patient population. We performed a retrospective cohort study of all DBE procedures performed at the University of Alabama at Birmingham between 11 January 2012 and 1 December 2020. The study received approval from the Institutional Review Board. The study population was found in the Provation database by searching for all DBE procedures during the 8-year time frame.

The criterion for inclusion in our study was a patient's first admission for overt obscure GI bleeding at our tertiary medical center. Those without previous EGD or colonoscopy to identify potential sources of bleeding were excluded from the study. Additionally, among those who received multiple DBE procedures, only the first procedure was included for analysis. Those below the age of 18 years and those who received DBE for any other reason were also excluded from the study. Patients were stratified into one of two groups based on the timing of DBE: within 72 h of GI bleed onset (emergent DBE) and beyond 72 h of GI bleed onset (nonemergent DBE). A diagram showing the inclusion criterion is shown in Figure 1.

Data collection. Data collection consisted of medical record chart view, for which data were filled in a password-protected, de-identified Excel document. Baseline patient information including age, sex, co-morbidities, and body mass index (BMI), as well as the use of anticoagulation or antiplatelet medications, was recorded. Procedure data included the type of procedure, total time of procedure (in minutes), anesthesia type, American Society of Anesthesiologists (ASA) classification, and whether the patient had a VCE prior to DBE. Diagnostic findings and therapeutic interventions were recorded from procedure data. Laboratory parameters at the time of admission were collected, which consisted of hemoglobin and hematocrit levels. The number of packed

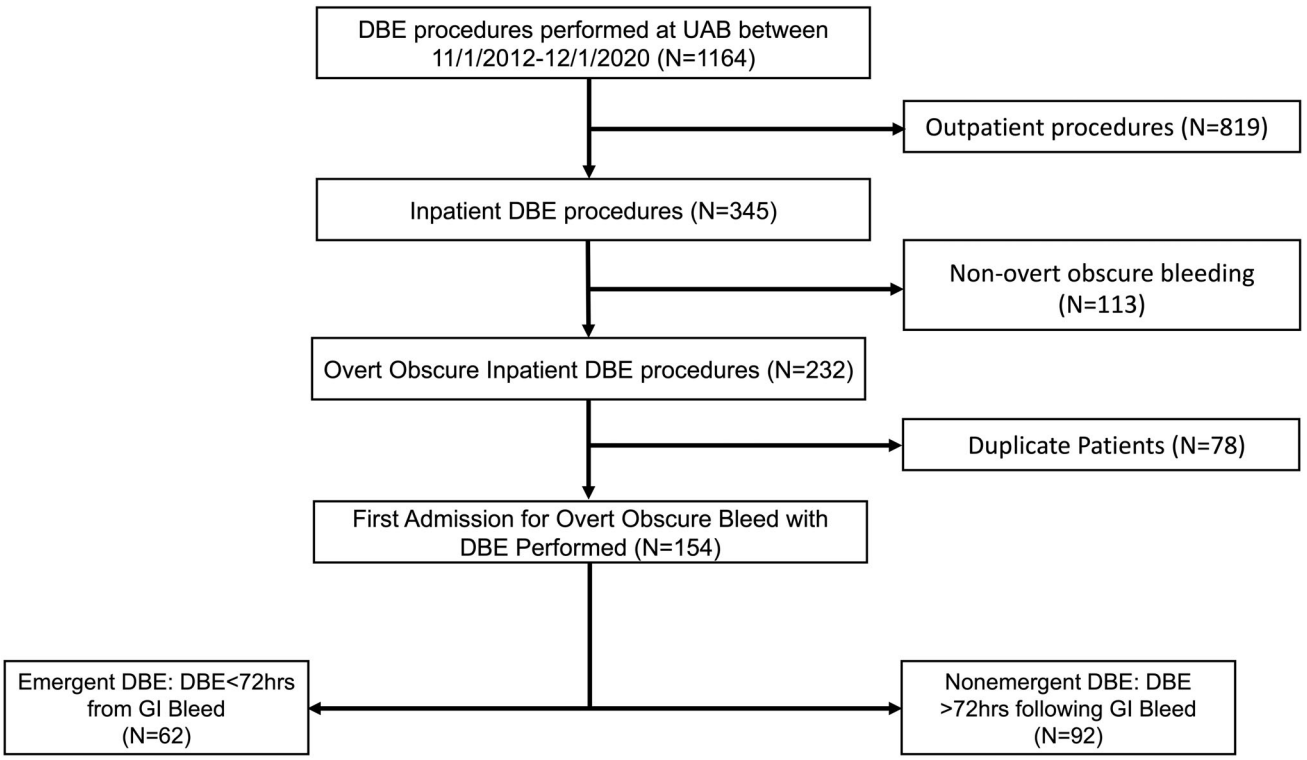

Figure 1 Patient flow inclusion diagram.

red blood cells (pRBCs) administered during the entire admission and any hemodynamic adverse events during the procedure were also recorded.

Diagnostic yield was defined as the ability to identify a culprit lesion, and therapeutic yield was defined as any intervention performed on the culprit lesion that led to a resolution of bleeding. Further outcome variables included 30-day re-admission and rebleed rates, 6-month re-admission and rebleed rates, overall rebleed rate, and overall mortality. Rebleed was defined by evidence of overt GI bleeding (hematochezia or melena) in the setting of a drop from baseline hemoglobin level.

Statistical analysis. All statistical analyses were performed with SAS version 9.4. Propensity score matching included sex, age, BMI, altered anatomy, ICU, retrograde *versus* anterograde approach, total procedure time in minutes, and VCE prior to DBE in the statistical model. Greedy nearest neighbor matching with a caliper of 0.5 for the logit of the propensity score as the distance metric[21] and exact matching for VCE prior to DBE were performed using SAS PROC PSMATCH. All analyses were conducted on both matched and unmatched samples.

Descriptive and outcome patient statistics were represented as means ± standard deviation (SD) for continuous variables or as a frequency percentage for categorical variables. Continuous and categorical variables were compared between groups using Student's independent-samples *t*-test and Pearson chi-squared test, respectively.

Univariate and multivariable logistic regression analyses were implemented to assess factors associated with overall diagnostic and therapeutic yield among the entire cohort. Backward variable selection was implemented for regression modeling, where a *P*-value <0.05 was deemed statistically significant.

Rebleeding post DBE was depicted through Kaplan–Meir survival curve analysis, which showed the probability of GI bleed-free survival analysis at different intervals of time following initial bleed. Survivability was compared between the two groups using the log rank test.

Results

Baseline patient information. A total of 154 patients met the inclusion criterion for our study, of which 62 had emergent DBE and 92 had nonemergent DBE. Baseline characteristics of the entire cohort before propensity score matching are shown in Table 1. Following exact propensity score matching for VCE, there were 56 patients each in the emergent and nonemergent groups. The matched samples had no significant difference in sex, age, BMI, surgically altered anatomy, end-stage renal disease (ESRD), and anticoagulation or antiplatelet use. Additionally, ASA subtype, anesthesia approach, retrograde *versus* anterograde approach, intensive care unit (ICU) admission, and total procedure time (in minutes) were similar between the two matched samples. Although mean hemoglobin (8.1 ± 1.7 *vs* 8.2 ± 2.0, $P = 0.74$) and hematocrit (24.2 ± 4.8 *vs* 24.6 ± 6.0, $P = 0.70$)

Table 1 Baseline characteristics of the entire patient population

Variable	Emergent DBE ($n = 62$)	Nonemergent DBE ($n = 92$)	*P*-value
Sex, male	34 (55%)	46 (50%)	0.556
Age, mean ± SD	63.4 ± 1.6	63.5 ± 1.5	0.976
BMI < 25, *n* (%)	15 (24%)	21 (23%)	0.844
ASA < 2, *n* (%)	3 (5%)	4 (4%)	0.866
Retrograde, *n* (%)	9 (15%)	17 (19%)	0.520
MAC anesthesia, *n* (%)	17 (27%)	22 (14%)	0.624
Surgically altered anatomy, *n* (%)	6 (10%)	15 (16%)	0.240
ESRD, *n* (%)	7 (11%)	14 (15%)	0.486
Hypertension, *n* (%)	43 (69%)	68 (74%)	0.382
Coronary artery disease, *n* (%)	26 (42%)	36 (39%)	0.727
Diabetes mellitus, *n* (%)	25 (40%)	33 (36%)	0.575
Cirrhosis, *n* (%)	7 (11%)	11 (12%)	0.899
Hyperlipidemia, *n* (%)	14 (23%)	26 (28%)	0.430
Chronic kidney disease, *n* (%)	16 (25%)	27 (29%)	0.631
COPD, *n* (%)	13 (21%)	6 (17%)	0.577
ICU admission, *n* (%)	17 (27%)	27 (29%)	0.795
Anticoagulation, *n* (%)	19 (30%)	21 (23%)	0.278
Antiplatelet, *n* (%)	24 (39%)	26 (28%)	0.174
Total procedure time, min	44.3 ± 3.2	43.6 ± 2.8	0.749
Hemoglobin, mean ± SD	8.0 ± 1.8	8.2 ± 2.1	0.595
Hematocrit, mean ± SD	24.0 ± 5.4	24.7 ± 6.2	0.481
Units of blood transfused, mean ± SD	3.4 ± 4.1	7.9 ± 6.8	0.000
VCE prior to DBE, *n* (%)	38 (61%)	65 (70%)	0.226
Weekend admission, *n* (%)	9 (15%)	14 (15%)	0.905

ASA, American Society of Anesthesiologists; BMI, body mass index; COPD, chronic obstructive pulmonary disease; DBE, double balloon enteroscopy; ESRD, end-stage renal disease; ICU, intensive care unit; MAC, monitored anesthesia care; SD, standard deviation. VCE, video capsule endoscopy.

upon presentation were similar between the groups, the mean number of units of blood transfused throughout the hospital stay was significantly higher in the nonemergent DBE group than in the emergent DBE group (7.6 ± 6.9 *vs* 3.2 ± 4.0, $P < 0.0001$) (Table 2).

Diagnostic and therapeutic yield. Within our matched cohort, diagnostic yield was higher in those who had emergent DBE than those who had nonemergent DBE (79% *vs* 57%, $P = 0.02$). Therapeutic yield also showed a similar trend, namely, higher in those with DBE within 72 h than those with DBE beyond 72 h (68% *vs* 43%, $P = 0.01$) (Table 3). Diagnostic findings and therapeutic interventions are given in Table 4.

Re-admission and GI Rebleed rate. There was no significant difference in 30-day or 6-month re-admission/rebleed rate between the two groups; however, the overall GI rebleed rate was significantly higher in those with nonemergent DBEs (45% *vs* 27%). Time to rebleed was also significantly shorter in the nonemergent group than in the emergent group (9.4 ± 8.6 months *vs* 14.8 ± 9.2 months, $P = 0.002$).

Logistic regression analysis. Univariate logistic regression analysis of the factors associated with diagnostic yield among the entire cohort showed that VCE and emergent DBE were significantly associated with increased diagnostic yield. This association remained statistically significant following multivariable analysis (odds ratio [OR]: 3.02, 95% confidence interval [CI]: 1.205–7.562, $P = 0.02$) and (OR: 3.01, 95% CI: 1.26–7.21, $P = 0.007$).

Logistic regression showed a significant association between VCE and emergent DBE with the overall therapeutic yield following univariate analysis. After controlling for cofounders through multivariable analysis, VCE (OR: 2.75, 95% CI: 1.12–6.73, $P = 0.03$) and emergent DBE (OR: 3.00, 95% CI: 1.34–6.73, $P = 0.007$) remained significantly associated with increased therapeutic yield. Multivariable analysis results for both diagnostic and therapeutic yield are shown in Table 5.

Table 2 Baseline variables of the matched sample (exact matching on Pill Cam)

Variable	Emergent DBE ($n = 56$)	Nonemergent DBE ($n = 56$)	*P*-value
Sex, male	23 (41%)	25 (45%)	0.7025
Age, mean ± SD	62.3 ± 12.4	63.5 ± 14.6	0.6500
BMI < 25, *n* (%)	14 (25%)	15 (27%)	0.8292
ASA < 2, *n* (%)	3 (5%)	3 (5%)	NA
Retrograde, *n* (%)	8 (14%)	7 (13%)	0.7814
MAC anesthesia, *n* (%)	16 (29%)	12 (21%)	0.3827
Surgically altered anatomy, *n* (%)	5 (9%)	7 (13%)	0.5412
ESRD, *n* (%)	7 (13%)	6 (11%)	0.7680
ICU admission, *n* (%)	15 (27%)	15 (27%)	NA
Anticoagulation, *n* (%)	15 (27%)	14 (25%)	0.8292
Antiplatelet, *n* (%)	18 (32%)	18 (32%)	NA
Total procedure time, min	44.3 ± 24.9	44.3 ± 27.7	0.9971
Hemoglobin, mean ± SD	8.1 ± 1.7	8.2 ± 2.0	0.7442
Hematocrit, mean ± SD	24.2 ± 4.8	24.6 ± 6.0	0.7024
Units of blood transfused, mean ± SD	3.2 ± 4.0	7.6 ± 6.9	<0.0001
VCE prior to DBE, *n* (%)	38 (68%)	38 (68%)	NA
Weekend admission, *n* (%)	9 (16%)	9 (16%)	NA

ASA, American Society of Anesthesiologists; BMI, body mass index; DBE, double balloon enteroscopy; ESRD, end-stage renal disease; ICU, intensive care unit; MAC, monitored anesthesia care; SD, standard deviation; VCE, video capsule endoscopy.

Table 3 Outcome variables of the matched sample (exact matching on video capsule endoscopy)

Variable	Emergent DBE ($n = 56$)	Nonemergent DBE ($n = 56$)	*P*-value
Diagnostic yield, *n* (%)	44 (79%)	32 (57%)	0.0152
Therapeutic yield, *n* (%)	38 (68%)	24 (43%)	0.0078
30-day re-admission, *n* (%)	7 (13%)	12 (21%)	0.2081
30-day rebleed, *n* (%)	6 (10%)	8 (14%)	0.5677
6-month re-admission, *n* (%)	15 (27%)	24 (43%)	0.0742
6-month rebleed, *n* (%)	8 (14%)	16 (29%)	0.0654
Overall rebleed, *n* (%)	15 (27%)	25 (45%)	0.0486
Time to rebleed, mean ± SD (months)	14.8 ± 9.2	9.4 ± 8.6	0.0018
Overall mortality, *n* (%)	7 (13%)	13 (23%)	0.1388
Hemodynamic complications, *n* (%)	3 (5%)	1 (2%)	0.3085

DBE, double balloon enteroscopy; SD, standard deviation.

Table 4 Diagnostic findings and therapeutic interventions of matched sample (exact matching on video capsule endoscopy)

Variable	Emergent DBE ($n = 56$)	Nonemergent DBE ($n = 56$)
Diagnostic yield, *n* (%)	44 (78.6%)	32 (57.1%)
Ulcer	10 (17.9%)	9 (16.1%)
Angioectasia/angiodysplasia	10 (17.9%)	5 (8.9%)
AVM	11 (19.6%)	11 (19.6%)
Dieulafoy	1 (1.8%)	2 (3.6%)
AVM/dieulafoy	3 (5.4%)	2 (3.6%)
Bleeding polyp	4 (7.1%)	2 (3.6%)
Other	5 (8.9%)	2 (3.6%)
Therapeutic yield, *n* (%)	38 (67.9%)	24 (42.9%)
APC	21 (37.5%)	10 (17.9%)
Epinephrine injection	4 (7.1%)	2 (3.6%)
Hemostatic clip	2 (3.6%)	2 (3.6%)
APC + hemostatic clip	1 (1.8%)	1 (1.8%)
Epinephrine injection + APC	1 (1.8%)	5 (8.9%)
Epinephrine injection + hemostatic clip	2 (3.6%)	1 (1.8%)
Epinephrine injection + hemostatic clip + APC	7 (12.5%)	3 (5.4%)

Abbreviations: APC, argon plasma coagulation; AVM, arteriovenous malformation; DBE, double balloon enteroscopy.

GI bleed-free survival analysis. Kaplan–Meier curve survival analysis conducted for GI bleed-free survival for the entire cohort up to 25 months post initial DBE procedure for OOGIB showed the survival trends between the two groups. Comparative analysis showed that those with DBE performed beyond 72 h of initial bleed had decreased GI bleed-free survival when compared to those with DBE performed within 72 h of initial bleed (Fig. 2). The difference in these GI bleed-free survival curves was determined to be statistically significant (log rank = 0.009).

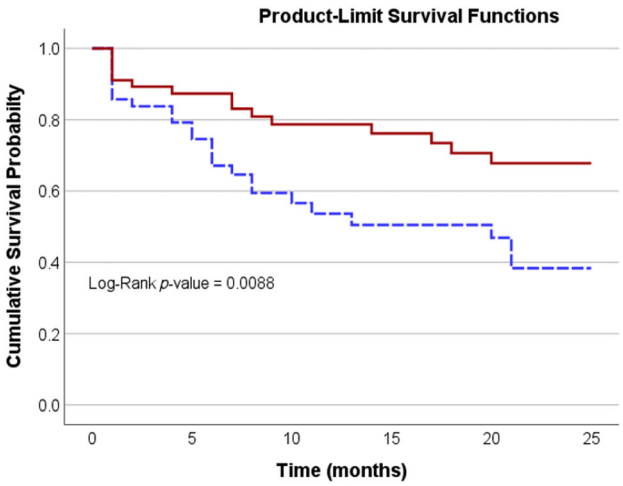

Figure 2 Kaplan–Meier curve for GI bleed-free survival up to 25 months following initial DBE. ⌐¬, nonemergent; ⌐¬, emergent.

Table 5 Univariate and multivariable logistic regression analysis of diagnosis and therapeutic yield with respect to video capsule endoscopy (VCE) and emergent double balloon enteroscopy (DBE)

Diagnostic yield	Univariate model			Multivariate model		
Variable	uOR	95% CI	*P*-value	aOR	95% CI	*P*-value
Age	1.002	0.973, 1.032	0.8979	0.995	0.962, 1.029	0.7591
Female	1.074	0.481, 2.398	0.8609	0.998	0.391, 2.545	0.9961
BMI < 25	1.687	0.644, 4.419	0.2868	1.607	0.574, 4.496	0.3665
ESRD	1.075	0.308, 3.754	0.9102	0.986	0.239, 4.074	0.9847
Procedure time	0.999	0.984, 1.014	0.9067	0.994	0.978, 1.011	0.5017
ICU admission	0.621	0.260, 1.484	0.2835	0.552	0.209, 1.455	0.2292
VCE	**2.684**	**1.164, 6.188**	**0.0205**	**3.018**	**1.205, 7.562**	**0.0184**
Emergent DBE	**2.750**	**1.200, 6.301**	**0.0168**	**3.010**	**1.257, 7.206**	**0.0134**
Therapeutic yield	**Univariate model**			**Multivariate model**		
Variable	uOR	95% CI	P-value	aOR	95% CI	*P*-value
Age	0.989	0.962, 1.018	0.4623	0.981	0.950, 1.014	0.2585
Female	1.235	0.580, 2.629	0.5834	1.196	0.496, 2.880	0.6903
BMI < 25	0.990	0.423, 2.317	0.9814	0.839	0.338, 2.085	0.7052
ESRD	0.658	0.206, 2.101	0.4799	0.516	0.144, 1.857	0.3113
Procedure time	1.006	0.991, 1.021	0.4150	1.003	0.987, 1.019	0.7143
ICU admission	0.894	0.386, 2.071	0.7944	0.901	0.354, 2.296	0.8278
VCE	**2.269**	**1.011, 5.091**	**0.0469**	**2.747**	**1.121, 6.729**	**0.0271**
Emergent DBE	**2.814**	**1.302, 6.085**	**0.0085**	**3.006**	**1.343, 6.728**	**0.0074**

Note: The numbers in bold indicate statistical significance.
Abbreviations: aOR, adjusted odds ratio; BMI, body mass index; ESRD, end-stage renal disease; ICU, intensive care unit; MAC, monitored anesthesia care; OR, odds ratio; SD, standard deviation; uOR, unadjusted odds ratio; VCE, video capsule endoscopy.

Discussion

OOGIB can be difficult to manage, with several patients often suffering from persistent bleeding despite multiple endoscopic and radiographic procedures. Our study investigated the role of emergent DBE in inpatient OOGIB to assess any impact on the overall diagnostic and therapeutic yield as well as rebleeding. Our results indicate that the timing of DBE may have significant impacts on the applicability of the procedure in an inpatient setting. In multivariable analysis, emergent DBE was associated with overall significantly higher diagnostic and therapeutic yield. Additionally, those who underwent nonemergent DBE required more units of packed red blood cells (pRBCs) throughout their admission and had an overall higher incidence of rebleeding post DBE. Those who underwent emergent DBE had higher GI bleed-free survival than those who had nonemergent DBE. Interestingly, VCE was also independently associated with higher diagnostic and therapeutic yield after multivariable analysis, indicating an important role of VCE in guiding DBE in OOGIB.

Our study adds to the growing body of literature that early timing of balloon-assisted enteroscopy from onset of bleeding can have positive impacts on therapeutic and diagnostic yield.[18,20,22–25] Various studies have assessed different periods, varying from within 24 h[22,24] to within 72 h from the onset of bleed.[20,23] A meta-analysis by Gomes et al. of 15 studies showed that emergent balloon enteroscopy was associated with overall higher diagnostic yield across all those studies. Conclusions regarding therapeutic yield were overall less concrete, given the heterogeneity among results.[26] Despite these previous reports, our study remains the largest single-center study in the United States to date to investigate the role of emergent DBE in inpatient OOGIB cases. By strictly focusing on DBE, we provide better insight in to the utility of DBE in such scenarios, whereas other published data have consisted mainly of single balloon enteroscopy (SBE) or a combination of SBE and DBE.

The positive impact on rebleeding among the emergent DBE group was demonstrated through fewer pRBC transfusions, decreased incidence of rebleeding, and longer GI bleed-free survival time following DBE. Other studies have analyzed the role of emergent DBE on rebleeding rates, and previously reported results are consistent with our findings.[18,23,27] Previously published data deduce that the first episode of rebleeding usually occurs within the first 3 years following enteroscopy.[27] Our study analyzed rebleeding rates up to a 25-month period post initial DBE, given the limitations in data availability. Overall, our results further demonstrate that emergent DBE can lead to higher therapeutic yield with overall benefits to prevent future rebleeding in these patients. Not only does this help improve patient outcomes, but from a monetary perspective, it can also reduce medical cost for both the patient and hospital system and also help prevent further re-admission for OOGIB, potentially obviating the need for repeat enteroscopy on an inpatient basis.

VCE used prior to DBE proved beneficial for overall diagnostic and therapeutic yield. Previous studies in emergent or urgent care setting have shown benefits for overall diagnostic yield with VCE prior to DBE[7,19,28]; however, whether VCE should be the first-line test before all OOGIB remains under question.[29] Aniwan et al. in their review of massive OOGIB showed that urgent (within 24 h) DBE had overall higher diagnostic yield than VCE.[30] Furthermore, Robles et al. report combining real-time VCE alongside DBE in urgent cases with diagnostic success and overall DBE management.[31] Our findings indicate that if VCE can be implemented prior to DBE either on an emergent or non-emergent basis, it can lead to improved diagnostic and therapeutic yield. The implementation of VCE prior to DBE requires tailoring toward each unique clinical scenario and the overall urgency and clinical parameters surrounding each bleed.

Our study is not without limitation. Foremost, the single-center design and the retrospective approach are limitations in themselves. Second, although the two groups were matched using propensity analysis, the selective single-center approach could have impacted the interpretation of our results. Additionally, the higher pRBCs transfusion requirement in the nonemergent group may represent more clinically severe GI bleeding, where emergent DBE may not be feasible. Although our sample size was relatively small ($n = 154$), our study is the largest single-center study to date in the United States to assess only DBE procedures of inpatient OOGIB. Compared to more recent studies, our population is of similar or even larger size with an adequate distribution of both emergent and control patients. Given our focus only on DBEs, our findings cannot be definitively applied to those who received other forms of enteroscopy (e.g. single balloon, spiral, etc.). Follow-up data were also limited to up to 25 months based on data availability for our patients.

The management of OOGIB remains a challenge, both in the inpatient and outpatient environment. Our findings reiterate the consensus of data that timing of DBE closer to onset of bleeding can lead to increased diagnostic and therapeutic success as well as decreased incidence of rebleeding. The role of VCE in such scenarios also remains a topic of discussion; however, our findings indicate that implementation of VCE prior to DBE is associated with increased diagnostic and therapeutic yield regardless of the enteroscopy timing. Further multicenter studies are needed to confirm these findings.

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