Original Article

The impact of inpatient capsule endoscopy on the need for therapeutic interventions in patients with obscure gastrointestinal bleeding

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Abstract

Background/Aim: There are limited data evaluating the impact of inpatient video capsule endoscopy (VCE) on the need for therapeutic interventions in hospitalized patients with obscure gastrointestinal bleeding (OGIB). The objective of this study was to determine the impact of inpatient VCE on the need for therapeutic interventions and rehospitalization for recurrent bleeding.

Patients and Methods: Hospitalized patients who underwent VCE for OGIB indication were retrospectively included. Clinical data were collected including therapeutic interventions performed after VCE. Specific therapeutic interventions were defined as the medical, endoscopic, or surgical treatment directly targeting the cause of OGIB. Patients were followed up to determine the rate of rehospitalization.

Results: A total of 48 inpatient VCE were identified, of which 43 VCE were performed for OGIB indication and were included for analysis. The completion rate and the diagnostic yield were 78.5% and 55.8%, respectively. Subsequent specific therapeutic interventions were performed in 65.2% and 5.8% of patients with positive and negative VCE, respectively ($P < 0.001$). After a median follow up of 30 months (minimum 12, maximum 58), rehospitalization for recurrent bleeding occurred in 30.4% and 17% of patients with positive and negative VCE, respectively. Patients with angiodysplasia on VCE were significantly more likely to be readmitted ($P = 0.02$). Throughout the course of the follow-up, only 2 (11.7%) patients with negative VCE underwent specific therapeutic interventions.

Conclusion: Inpatient VCE is an effective tool to identify patients who need specific therapeutic interventions. Patients with negative VCE are unlikely to be readmitted or require specific therapeutic interventions in the index admission.

Keywords: Capsule endoscopy, device-assisted enteroscopy, obscure gastrointestinal bleeding

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INTRODUCTION

Obscure gastrointestinal bleeding (OGIB) accounts for 5% of all cases of gastrointestinal bleeding and in about 75% of cases, it originates from a small bowel source.[1] Compared to non-obscure gastrointestinal

Access this article online	
Quick Response Code:	Website: www.saudijgastro.com
	DOI: 10.4103/sjg.SJG_415_19

How to cite this article: Alsahafi M, Cramer P, Chatur N, Donnellan F. The impact of inpatient capsule endoscopy on the need for therapeutic interventions in patients with obscure gastrointestinal bleeding. Saudi J Gastroenterol 2020;26:53-60.

bleeding, OGIB is associated with the utilization of more hospital resources, recurrent hospital admissions and overall increased healthcare cost. Several techniques are available to investigate the source of OGIB including push enteroscopy, video capsule endoscopy (VCE), device assisted enteroscopy (DAE), CT enterography (CTE), CT angiography, magnetic resonance enterography (MRE) in addition to intraoperative endoscopy. Because of the non-invasive nature and the high diagnostic yield, VCE has revolutionized the management of OGIB and is currently recommended as the first line diagnostic test for patients with OGIB.[2-4] Depending on the result of VCE, patients may undergo further diagnostic investigations and/or therapeutic interventions.

The impact of VCE on the management of patients with OGIB has been the focus of many studies since the introduction of VCE in 2001. Most of the published studies included VCE performed in an outpatient setting or included a mixed patient population in which only a smaller proportion of inpatients were included but not separately analyzed.[5-17] The results of these studies may not be generalizable to the inpatient population for two reasons. First, the diagnostic performance of VCE could be different when performed in hospitalized patients. While the completion rates for inpatient VCE is known to be lower,[18,19] the diagnostic yield is optimized by having the VCE done soon after the onset of bleeding.[13,19] Second, the clinical characteristics of patients hospitalized with OGIB, such as medical comorbidities, and the nature of the bleeding events including the severity of presentation are likely to be different.

In this study, we aimed to determine the impact of VCE on the need for therapeutic interventions for hospitalized patients with OGIB. We also aimed to determine the rate of recurrent bleeding resulting in repeated hospitalization.

PATIENTS AND METHODS

Patients

The study was approved by the University of British Columbia Clinical Research Ethics Board and the Vancouver Coastal Health Research Institute. We included all hospitalized patients who underwent VCE for OGIB indication at Vancouver General Hospital, a tertiary academic center and the largest hospital in British Columbia, Canada. Inpatient VCE were identified through a prospective capsule endoscopy database that includes data related to all patients who underwent VCE at our center. The database includes information related to patients' demographics, indication for VCE, use of a prokinetic drug, and completeness of small bowel examination. Patients were excluded if the VCE were performed in an outpatient setting or if the indication for VCE was not OGIB.

Clinical and laboratory data were collected from the prospective capsule endoscopy database and by retrospectively reviewing the electronic hospital records.

VCE procedure

Prior to January 2015, all VCE studies were performed using Endocapsule 1 (Olympus, Tokyo, Japan). Later, all VCE studies were performed using Pillcam SB3 (Given Imaging, Yoqneam, Israel). All patients were instructed to follow a clear liquid diet after lunch the day prior to VCE, followed by an overnight fast after midnight. They were permitted to resume a clear fluid diet and to have a light meal 2 and 4 h after the beginning of recording, respectively. All patients were given 2 L of polyethylene glycol solution for bowel preparation on the evening before the VCE procedure day, 1 L at 6 pm and 1 L at 10 pm. Prucalopride was given routinely for all patients who had VCE done after March 2014 as per our protocol after this date. No other prokinetic drugs were given. The VCE recorder was disconnected after 8 h of recording. One of two gastroenterologists with experience in VCE reviewed the VCE recordings.

Definitions

In this study, OGIB was defined as gastrointestinal bleeding of the unclear source after negative esophagogastroduodenoscopy (EGD) and colonoscopy (CLN). Overt bleeding was defined as visible bleeding episodes manifested by melena, hematochezia, and/or hematemesis at the time of hospital admission or during hospitalization. Occult bleeding was defined as unexplained iron deficiency anemia with or without positive fecal occult blood testing.

We graded VCE findings based on the P0-P2 grading system previously reported.[20] The VCE study was considered positive if a significant lesion (P2) was seen anywhere in the gastrointestinal tract and thought to be the source of the OGIB including angiodysplasia, ulcers, or mass lesions. The presence of fresh blood was considered as a positive finding as this indicates the site of OGIB and facilitates further management. Alternatively, the VCE study was considered negative if no abnormality was found (P0) or an abnormality of uncertain significance was seen (P1). Abnormalities of uncertain significance included mucosal red spots and small isolated erosions. The small bowel completion rate was defined as the proportion of VCE

studies in which the cecum was reached, excluding cases in which VCE was retained due to small bowel strictures. Diagnostic yield was defined as the proportion of VCE studies that were positive.

Management after VCE

After VCE, patients were divided into two groups depending on whether further endoscopic and/or radiological workup was done. Further workup aimed to provide therapeutic interventions for patients with positive VCE or to identify the source of OGIB in patients with negative VCE. Moreover, management after VCE was divided into non specific or specific therapeutic interventions. Non specific therapeutic interventions were defined as supportive treatment, as needed, including iron replacement, blood transfusion and discontinuation/interruption of antiplatelets or anticoagulants. Specific therapeutic interventions were defined as interventions directly targeting a specific cause of OGIB with or without supportive treatment. Examples of specific therapeutic interventions include argon plasma coagulation for angiodysplasia, surgical resection for tumors and specific drug therapies such as chemotherapy for small bowel lymphoma. Therapeutic interventions were included if they were performed during the index hospital admission or planned during the admission and performed shortly, within 2 weeks, after discharge. For DAE, our usual practice is to choose the antegrade DAE route if the suspected pathology area is within the proximal 70% of the SBTT, and the retrograde route when the suspected pathology is within the distal 30% of the SBTT. The hospital electronic medical records were reviewed to collect data on rebleeding event resulting in rehospitalization. Follow-up period was defined as the period from the date of the index hospital admission to the end of the study.

Statistical analysis

The mean and standard deviation and/or the median with range were used for continuous variables as appropriate. The percentage and count were used for categorical variables. In this study, three patients had a repeat VCE done (one for prior gastric retention, one for persistent bleeding despite therapy, and one for incomplete VCE). To help with analysis, the outcome for patients who had repeat VCE was categorized based on the combined results of the two VCE, while diagnostic yield and completion rate were assessed separately for each individual VCE. Statistical analysis for categorical variables was performed using the Chi-square test or Fisher's exact test as appropriate. A *P*-value of less than 0.05 was considered statistically significant.

RESULTS

Baseline characteristics

A total of 320 VCE were performed at our center between November 2011 and September 2015, of which 48 were done in hospitalized patients. Of the 48 inpatient VCE, 5 were done for non - OGIB indications and were excluded. Therefore, a total of 43 inpatient VCE, performed in 40 patients, were finally included in this study. The baseline characteristics for patients are shown in Table 1. The mean patient's age was 62.7 (+/- 15.4) years. Seventy two percent of the patients were male. The indication for VCE was overt bleeding in 41 and occult bleeding in 3 patients. Twenty-two patients received a 2 mg single dose of prucalopride at the time of VCE ingestion. In 6 VCE studies, endoscopic placement into duodenum was performed. Investigations, other than EGD and CLN, performed to investigate for the source of OGIB prior to VCE are shown in Table 2.

Findings

Incomplete gastric passage occurred in one VCE study. One VCE was retained secondary to an ischemic small bowel stricture, which was the source of OGIB. After excluding this VCE retention case, the cecum was reached

Table 1: Baseline Characteristics of patients (*n*=40)

Characteristic	*n*
Age mean, Y (sd)	62.7 (15.4)
Male	29 (72.5%)
Female	11 (27.5%
Medical comorbidities	
Cardiac disease	15 (37.5%)
Congestive heart failure	4 (10%)
Valvular heart disease	11 (27.5%)
Stroke	5 (12.5%)
Chronic kidney disease	2 (5%)
Chronic lung disease	3 (7.5%)
Liver cirrhosis	3 (7.5%)
Hemoglobin nadir mean g/L (sd)	71.07 (18.92)
ASA	15 (37.5%)
Plavix	4 (10%)
NSAIDS	3 (7.5%)
Warfarin	6 (15%)
Heparin	0 (0%)
Neo-oral anticoagulants	1 (2.5%)

Table 2: Investigations performed prior to VCE, other than EGD and CLN

Investigation	23 Patients with positive VCE	17 Patients with negative VCE	*P*
Push enteroscopy	1	4	0.15
CT Enterography	7	2	0.25
CT angiography	6	7	0.31
Red blood cell scan	4	3	1
Meckel's scan	1	0	1
Device assisted enteroscopy	1	0	1

VCE: Video capsule endoscopy; EGD: Esophagogastroduodenoscopy; CLN: Colonoscopy; CT: Computed tomography

in 33 out of 42 VCE studies, with an overall small bowel completion rate of 78.57%. The completion rate was higher for patients who received prucalopride (90.4%, 19/21 vs. 61.9%13/21%, $P = 0.06$). Only 2 of the 6 endoscopically placed VCE reached the cecum. When the endoscopically placed capsules and the capsule that was retained in the small bowel were excluded, the completion rate was 83.3%. Of all VCE studies, 24 VCE were positive which resulted in a diagnostic yield of 55.8%. Of the 24 positive VCE studies, 2 VCE showed positive findings in the stomach, 21 in the small bowel, and 1 in the cecum.

Of patients with positive small bowel findings, angiodysplastic lesions were the most common (52.3%, $n = 11$), followed by fresh blood of unclear source (23.8%, $n = 5$), ulcers (19%, $n = 4$), and mass lesions (4.7%, $n = 1$). The two positive findings in the stomach were: fresh blood with the source later identified on a repeat EGD to be a hyperplastic polyp and gastric antral vascular ectasia. The only positive colon finding was cecal angiodysplasia. Of all patients with positive VCE findings; 5 patients (20.8%) had a bleeding source in the stomach or duodenum within the reach of a standard gastroscope, of which, 2 angiodysplastic lesions were found in the duodenum and 1 duodenal ulcer in addition to the two above mentioned gastric findings.

Management after VCE

Overall, 23 patients had positive VCE and 17 patients had negative VCE. The performance of further endoscopic and/or radiological workup after VCE is shown in Table 3. Among patients with positive VCE, 82.6% underwent further workup while 17.39% received non specific therapeutic interventions without further workup. Among patients with negative VCE, 23.52% of patients underwent further workup while 76.47% received non specific therapeutic interventions without further workup. Patients with positive VCE were significantly more likely to undergo further workup compared to patients with negative VCE, $P < 0.001$. Among workup performed after VCE, DAE was the most common procedure. For the 10 patients who had DAE, 9 patients had single balloon enteroscopy while 1 patient had, through the scope, balloon-assisted deep enteroscopy.

Table 3: Workup performed after VCE

	23 patients with positive VCE	17 patients with negative VCE
Further investigations*	19 (82.60%)	4 (23.52%)
EGD	4	2
CLN	2	0
CT enterography	1	1
CT angiography	0	0
Push enteroscopy	3	1
Device assisted enteroscopy	9	1
Intraoperative enteroscopy	1	0

*A patient may undergo more than one type of intervention.
VCE: Video capsule endoscopy; EGD: Esophagogastroduodenoscopy; CLN: Colonoscopy; CT: Computed tomography

Among the 4 patients with negative VCE who underwent further workup, only 1 patient had a bleeding source identified. This patient had progressive bleeding after VCE and was later diagnosed on EGD to have ischemic gastritis.

Therapeutic interventions after VCE

Figure 1 summarized the outcome after VCE including the type of therapeutic interventions performed. For patients with positive VCE, specific therapeutic interventions were performed in 15 patients which constituted 65.2% of all patients who had positive VCE, and 78.9% of the subgroup that underwent further workup. For patients with negative VCE, specific therapeutic interventions were performed only in 1 (5.8%) patient. Patients with positive VCE underwent more specific therapeutic interventions compared to those with negative VCE ($P < 0.001$).

Among all patients included in this study, 10 patients underwent DAE (9 after positive VCE and 1 after a negative VCE but a prior CTE suggesting a distal ileal polyp). Positive findings were identified in 7 patients, all underwent specific therapeutic interventions which resulted in a diagnostic and therapeutic yield of 70% for DAE. For the 3 patients who did not undergo specific therapeutic interventions, the area of small bowel pathology was presumed to be not reached and these patients were managed conservatively.

Rehospitalization for recurrent bleeding

Patients were followed for a median of 30 months (minimum 12, maximum 58). Figure 2 summarized the rehospitalization events according to the result of initial VCE and whether specific therapeutic interventions were performed in the initial presentation. Rehospitalization occurred in 3 (17.6%) out of the 17 patients who had initial negative VCE versus 7 (30.43%) out of the 23 patients who had initial positive VCE.

Among the 3 patients with negative VCE in the index admission, further diagnostic workup after readmission led to specific diagnosis and therapeutic interventions in only 1 patient. This patient was diagnosed with an ileal carcinoid tumor and underwent surgical treatment. This patient had CTE in the initial admission suggesting a distal ileal polyp but a retrograde DAE did not identify the lesion, presumably, the area harboring the lesion was not reached. The remaining 2 patients had no identifiable source of bleeding. Throughout the course of this study, including

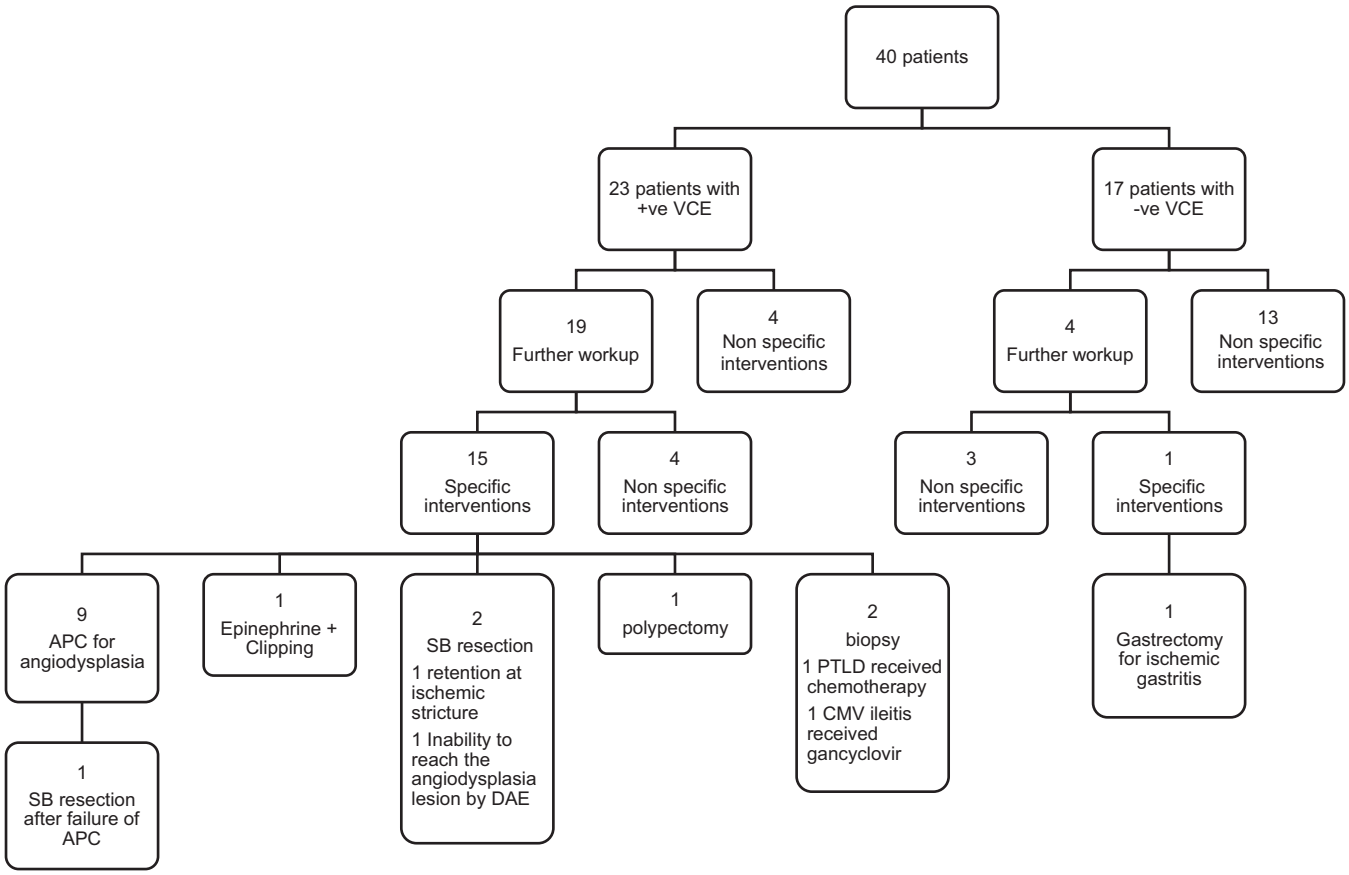

Figure 1: Management after video capsule endoscopy in the initial admission. *VCE, video capsule endoscopy; APC, argon plasma coaglation; SB, small bowel; DAE, device assisted enteroscopy; PTLD, post-transplant lymphoproliferative disorder; CMV, cytomegalovirus*

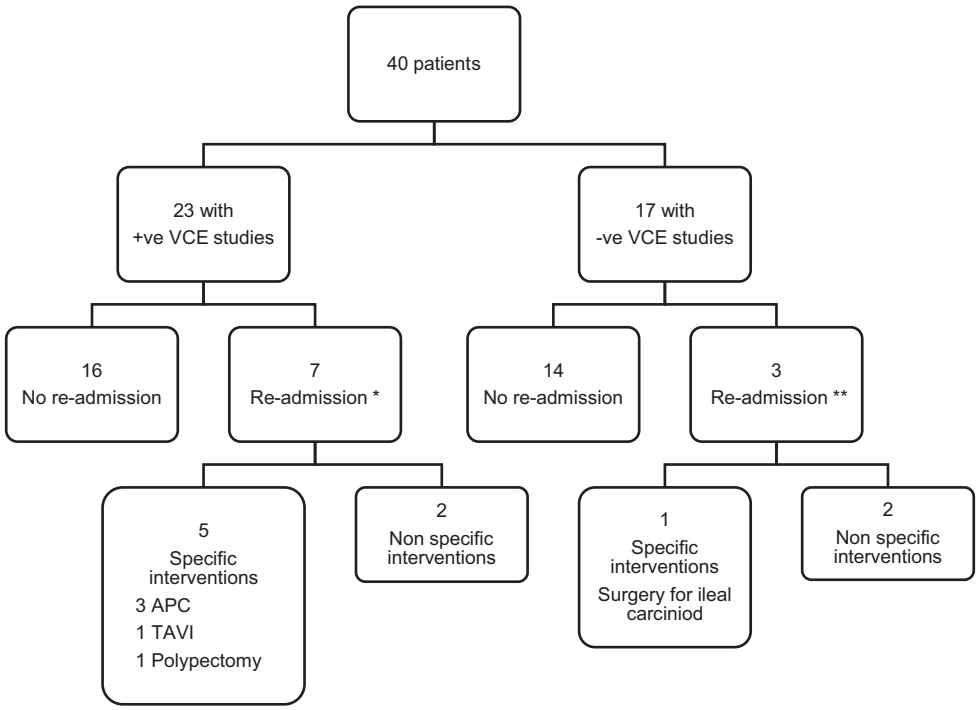

Figure 2: Rehospitalization and therapeutic interventions for recurrent bleeding. *VCE, video capsule endoscopy; APC, argon plasma coagulation; TAVI, trans-catheter aortic valve replacement.* *Five of 7 patients had prior specific therapeutic interventions. **None had prior specific therapeutic interventions

initial hospital admission and follow up, only 2 (11.76%) patients of the 17 patients with negative VCE had a specific therapeutic intervention performed.

Of the 7 patients with initial positive VCE who had readmission, 6 had similar diagnosis (5 recurrent angiodysplastic lesions, 1 regrowth of gastric antral hyperplastic polyp) and 1 had a new diagnosis (peri-stomal varices). Patients with angiodysplastic lesions on VCE were significantly more likely to be readmitted for recurrent bleeding compared to other positive VCE findings ($P = 0.02$).

DISCUSSION

Historically, inpatient capsule endoscopy has been compared less favorably to outpatient capsule endoscopy due to the lower completion rates and suboptimal bowel preparation. In our study, we found the diagnostic performance of inpatient VCE to be comparable to outpatient VCE. Our results showed that VCE significantly impacted the management of inpatients with OGIB. More importantly, the findings of VCE effectively guided the need for therapeutic interventions in hospitalized patients.

The diagnostic yield of VCE in our inpatient population was 55%. This is similar to a previous study that found the diagnostic yield to be 48% for inpatient VCE, compared to 37% for outpatient VCE.[19] Another study found positive findings in 65% of inpatient VCE examinations compared to 53% in the outpatient setting.[13] A previous meta-analysis that included inpatient and outpatient population concluded a pooled diagnostic yield of 60%.[21] However, there was heterogeneity in defining the diagnostic yield between the included studies. In our study, we excluded lesions of uncertain significance from positive findings. An advantage of performing VCE soon after the onset of the bleeding event is the higher probability of identifying pathology.[13,19] VCE performed during the bleeding event has the advantage to detect fresh blood which localizes the bleeding site and helps to select the appropriate subsequent intervention. In our study, fresh blood was the second most common finding, 22% of positive VCE studies. A previous study found fresh blood as the most common finding in the inpatient population.[13] In 25% of the positive VCE studies, the bleeding lesions were identified in a location within the reach of EGD or CLN. It is not uncommon to have lesions missed or underestimated to be the cause of bleeding.[22] Therefore, it should be considered to repeat the EGD and/or the CLN depending on the quality of previous procedures.

In the current study, the overall small bowel completion rate was 78%. This completion rate is higher than what was previously reported for inpatient VCE and comparable to the completion rate for outpatient VCE.[18,19,21] The completion rate was 90% in the group that received prucalopride versus 61% in the group who did not receive prucalopride ($P = 0.06$), suggesting that prucalopride could be a simple intervention to increase the completion rate for hospitalized patients, as we have shown in a previous study.[23] While the endoscopic placement of the VCE is known to improve the completion rates, only 2 of the 6 endoscopically placed VCE reached the cecum in our study reflecting the fact that gastric passage is only one of many factors that affect the completion rates.[24] Patients who require endoscopic placement could be at a higher risk of slow small bowel transit given their underlying medical comorbidities. Furthermore, procedural sedation used during endoscopic placement may have a negative impact on small bowel transit time.[25] Using the new generation VCE with longer battery life, encouraging patient mobilization and possibly the use of prokinetic drugs may help to limit the incomplete small bowel examination.

The rate of specific therapeutic interventions was significantly higher among patients with positive VCE ($P < 0.001$). Specific therapeutic interventions were performed in 65.2% of patients with positive VCE, versus 5.8% of patients with negative VCE ($P < 0.001$). The therapeutic yield for DAE following positive VCE was 70%. The rate of endoscopic and surgical therapeutic interventions among patients with positive VCE in our study is within the range of previously published studies.[13,14]

When evaluating for the risk of rebleeding resulting in repeated hospitalization, our study suggests a favorable outcome for patients who had negative VCE. While 17% of patients with negative VCE had recurrent admission, only 11% required endoscopic or surgical therapeutic intervention throughout the course of initial presentation and follow up. A recent meta-analysis that included 26 studies found a pooled rebleeding rate of 19%, which is similar to our results.[12] In our study, one of the three patients with negative VCE who had repeated hospitalization for recurrent bleeding was subsequently diagnosed with an ileal carcinoid tumor. In a comparative retrospective study that included 17 patients with small bowel tumors, CTE detected the lesion in 16 of 17 patients (94.1%), and VCE detected the lesion in only 6 of 17 patients (35.3%).[26] Although small bowel tumors are rare causes for OGIB, CTE should be considered for patients who continue to bleed

despite having a negative CE. This is particularly relevant for young patients with no risk factors for small bowel ulcers or angiodysplasia.

Patients with positive VCE are at risk of recurrent bleeding despite having received prior endoscopic therapeutic interventions. Seven of 23 (30%) patients with positive VCE had recurrent bleeding requiring hospital admissions, despite prior therapy being performed in 5 of them. Previously published studies that included a proportion of inpatients found a rebleeding rate of 20–34% after positive VCE.[14,15] Predictably, angiodysplasia was the most common diagnosis in patients with recurrent bleeding. This is explained by the recurrent nature of the vascular lesions, and in some cases lesions could be missed by VCE or difficult to reach by DAE.

Several factors should be considered when deciding between inpatient and outpatient VCE. With the higher diagnostic yield with the early performance of VCE, inpatient VCE is preferred over outpatient VCE. However, the performance of inpatient VCE may be associated with an increased healthcare cost in a group of stable patients who may otherwise be discharged. In a recent study, it was suggested that there is cost saving with the performance of VCE in an outpatient setting.[27] Another study, however, suggested a decrease in the length of hospital stay with the early performance of VCE.[13] The optimal strategy is likely to be discharging stable patients home with rapid access to outpatient VCE and subsequent therapeutic intervention if needed, following discharge. Hence, the diagnostic yield would not be significantly jeopardized.

We recognized several limitations of our study. The study has the inherent limitations of the retrospective study design. We included only patients who had VCE performed. The selection of patients for VCE was at the discretion of the gastroenterologist involved in the case. Although we had a small number of patients, this is the first study to specifically focus on the impact VCE on the need for therapeutic interventions for the inpatient population, with follow-up data on the need for repeated hospitalization. We did not include data on the quality of bowel preparation as there was no standard method followed in the VCE reporting during the study period. Given the inpatient nature of the study, the bowel preparation could have been poor, yet the VCE could be positive by detecting active small bowel bleeding. Another limitation of this study is that we could not collect data on rebleeding events that did not require hospital admission, such as, occult bleeding requiring outpatient iron supplementation.

In conclusion, VCE significantly impacts the management of hospitalized patients with OGIB. Inpatient VCE is an effective tool to select patients for therapeutic interventions. Inpatients with OGIB who have negative VCE studies are unlikely to require specific therapeutic interventions. Therefore, expectant management should be the general approach for most of these patients.

Authors contribution

Majid Alsahafi contributed to study concept, design, data acquisition, analysis, interpretation and drafting the manuscript, Paula Cramer contributed to study concept and data acquisition, Nazira Chatur contributed to study concept and design, Fergal Donnellan contributed to study concept, design and interpretation. All authors reviewed the manuscript for critical revision and approved the final version.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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