## **ORIGINAL ARTICLE**



# Patients on Antithrombotic Agents with Small Bowel Bleeding –Yield of Small Bowel Capsule Endoscopy and Subsequent Management

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#### **Abstract**

**Background and Aims** Small bowel gastrointestinal bleeding (GIB) is associated with multiple blood transfusions, prolonged and/or multiple hospital admissions, utilization of significant healthcare resources, and negative effects on patient quality of life. There is a well-recognized association between antithrombotic medications and small bowel GIB. We aimed to identify the diagnostic yield of small bowel capsule endoscopy (SBCE) in patients on antithrombotic medications and the impact of SBCE on treatment course.

**Methods** The electronic medical records of nineteen hundred eighty-six patients undergoing SBCE were retrospectively reviewed.

Results The diagnostic yield for detecting stigmata of recent bleeding and/or actively bleeding lesions in SBCE was higher in patients that were on antiplatelet agents (21.6%), patients on anticoagulation (22.5%), and in patients that had their SBCE performed while they were inpatient (21.8%), when compared to the patients not on antiplatelet agents (12.1%), patients not on anticoagulation (13.5%), and with patients that had their SBCE performed in the outpatient setting (12%). Of 318 patients who had stigmata of recent bleeding and/or actively bleeding lesion(s) identified on SBCE, SBCE findings prompted endoscopic evaluation (small bowel enteroscopy, esophagogastroduodenoscopy (EGD), and/or colonoscopy) in 25.2%, with endoscopic hemostasis attempted in 52.5%.

**Conclusions** Our study, the largest conducted to date, emphasizes the importance of performing SBCE as part of the evaluation for suspected small bowel bleeding, particularly in patients taking antithrombotic therapy, and especially during their inpatient hospital stay.

**Keywords** Gastrointestinal bleeding · Antithrombotic · Capsule endoscopy · Antiplatelet agents · Anticoagulation · Inpatient

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## Introduction

In patients who present with gastrointestinal bleeding (GIB), initial evaluation (including bi-directional endoscopy with esophagogastroduodenoscopy [EGD] and colonoscopy) fails to identify the source of bleeding in 10–20% of cases [1]. In approximately half of these cases, recurrent or persistent bleeding occurs. Due to advances in small bowel imaging (including small bowel capsule endoscopy [SBCE], angiography, and device-assisted enteroscopy [DAE]), a bleeding source that has not been identified on bi-directional endoscopy is likely to be identified in the small bowel in most cases [2].

Antithrombotic medications are some of the most commonly prescribed drugs in the United States, and the number of prescriptions is increasing [3]. This pharmacologic



class includes medications classified as anticoagulants or antiplatelet agents [4]. Antithrombotic medications can exacerbate bleeding from pre-existing lesions in the GI tract. Studies show that antiplatelet medications, aspirin specifically, can even cause direct mucosal injury [5–8]. The risk of GIB increases up to 10% for patients prescribed antithrombotic therapy, and the annual risk of upper GIB may be as high as 4.5% [9].

The American College of Gastroenterology (ACG) and the American Society for Gastrointestinal Endoscopy (ASGE) clinical guidelines recommend SBCE as the first line procedure for evaluation of the small bowel [2, 10]. SBCE is a minimally invasive, well-tolerated diagnostic tool that allows visualization of the entire small bowel without exposing the patient to additional risks, such as sedation [11, 12]. Of note, we prefer the term SBCE as opposed to video capsule endoscopy (VCE) as VCE can refer to any type of capsule endoscopy, including esophageal capsule endoscopy, SBCE, colon capsule endoscopy, and small bowel - colon capsule endoscopy. The diagnostic yield of SBCE is comparable with DAE [13, 14]. The most common lesions associated with small bowel bleeding are erosions, ulcers, and vascular lesions [15-17]. Older age, warfarin and chronic liver disease are associated with higher capsule endoscopy yield [18].

We aimed to identify the yield of SBCE in patients taking antithrombotic medications that had SBCE performed while they were inpatient, but also SBCE performed in the outpatient setting, and the impact these findings had on the patients' treatment in the post-SBCE period.

## Methods

The electronic medical records (EMRs) of 1986 patients were retrospectively reviewed. These patients underwent SBCE between 2002 and 2021 at a tertiary care center in Cleveland, Ohio. This study received Case Western Reserve University/University Hospitals Cleveland Medical Center IRB approval.

Patients were separated into two cohorts: those who had stigmata of recent bleeding and/or actively bleeding lesion identified on their SBCE and those who did not. The SBCE findings were graded by using the Saurin classification/score. <sup>19</sup> The Saurin classification divides SBCE lesions into three levels of bleeding risk, P0, P1, and P2. P0 are lesions without hemorrhagic potential (for example erythematous patch, diverticula without the presence of blood, nodules without mucosal breaks), P1 are lesions with intermediate (for example red spots, small or isolated erosions), and P2 are lesions with high hemorrhagic potential (for example angioectasias, ulcerations, tumors, or varices).

This score has been validated, and it has been recommended as a useful tool in the setting of small bowel bleeding by the European Society of Gastrointestinal Endoscopy (ESGE) [14, 20].

EMRs were reviewed to obtain demographic information and body mass index (BMI). ICD-9/10 diagnostic codes were used to identify pre-specified comorbidities selected due to possible increased risk of GIB. These comorbidities included: chronic kidney disease (CKD), dialysis requirement, atrial fibrillation, aortic stenosis (AS), history of heart valve replacement (both surgical and transcatheter aortic valve replacement), cirrhosis, and medications from one month prior to the procedure up to on the day of procedure. Antiplatelet therapy included aspirin, clopidogrel, and ticagrelor, and anticoagulation therapy included enoxaparin, warfarin, apixaban, and rivaroxaban. Additionally, we reviewed SBCE reports to identify whether the procedure was performed in the outpatient or inpatient setting.

For those patients that had stigmata of recent bleeding and/or actively bleeding lesion/s identified on SBCE, the EMR was reviewed to identify events occurring after SBCE, including endoscopic procedures (repeat SBCE, enteroscopy, EGD, and colonoscopy), endoscopic therapy, radiologic evaluation (computed tomography angiography [CTA], tagged red blood cells scan, and Meckel's scan), hospitalization rate for recurrent GIB episodes, repeat SBCE, surgery, prescription of octreotide for angioectasias, prescription of proton pump inhibitors (PPI) for erosion/s and/or ulcer/s, and discontinuation of antithrombotic therapy. In this cohort, recurrent GIB episodes and cardiovascular events (myocardial infarction, cerebral vascular attack, and limb ischemia) where identified up to 4 years post-SBCE.

## **Statistical Analysis**

Patients' demographic characteristics and clinical factors were summarized as mean, standard deviation (SD), range (minimum, maximum) for continuous variables, and frequency (percent [%]) for categorical variables. Demographic variables were compared between the groups using the independent two-sample T-test for continuous measurements and Chi-square test for categorical factors. Generalized estimating equations (GEE) logistic regression that takes potential correlation of outcomes from the same patients into account was used to identify risk factors related to the binary outcomes [21]. First, univariable GEE logistic regression was performed to identify associations of outcomes with each demographic and clinical factor as a predictor. Next, using multivariable GEE logistic regression, significant predictors from the univariable GEE logistic regression were tested adjusting the effects of demographic variables (specifically age, race, and gender).



All tests are two-sided, and *p*-values less than 0.05 were considered statistically significant. Data were analyzed using Statistical Analysis Software (SAS) version 9.4 (SAS Institute, Inc., Cary, NC).

## **Results**

Over the 19-year period, a total of 2160 SBCE were performed (Table 1). Among these, 130 patients underwent more than one SBCE. The overall yield of all patients undergoing SBCE was 14.7% for detecting lesions with stigmata of recent bleeding or active bleeding. In patients being treated with one or more antiplatelet agents, the yield was 21.6%. In patients that were on anticoagulation, the overall yield of SBCE for detecting stigmata of recent bleeding and/or actively bleeding lesions was 22.5% (Table 2).

Of the total number of patients, 39.6% (n=536) were prescribed an antiplatelet agent. Specifically, of these patients, 34.3% (n=456) were taking aspirin 81 mg (higher doses of aspirin were not included in this study), 10.2% (n=136) were taking clopidogrel, and 0.8% (n=10) were taking ticagrelor. 90 patients (6.8%) were taking dual-antiplatelet therapy (DAPT, i.e., aspirin plus either clopidogrel or ticagrelor). Of the total number of patients, 22.6% (n=302) were prescribed anticoagulation. Of these 2.2% (n=29) were taking enoxaparin, 14.9% (n=199) were taking warfarin, 3.1% (n=42) were taking apixaban, and 3.7% (n=49) were taking rivaroxaban. 136 (10.1%) were being treated with both an antiplatelet agent and anticoagulation (Table 3).

14.7% of patients (n=318) had a lesion identified on SBCE that had stigmata of recent bleeding and/or active bleeding. These patients were more likely to be older than 60 (odds ratio (OR)=1.025, 95% CI [1.017–1.034]; p<0.001), have at least one comorbidity (OR=2.141, 95% CI [1.597–2.870; p<0.0001), and have a diagnosis of either atrial fibrillation (OR=1.686, 95% CI [1.183–2.401; p=0.003) and AS (OR=2.288, 95% CI [1.326–3.948; p=0.002). These patients were more likely to be treated with an antiplatelet agent (OR=2.007, 95% CI [1.568–2.569]; p<0.0001). They were more likely to be on anticoagulation (OR=1.703, 95% CI [1.236–2.347]; p=0.001). These patients were more likely to be treated with both an antiplatelet agent and be anticoagulated (OR=2.426, 95% CI

[1.529–3.848]; p = 0.002). Lastly, identification of stigmata of recent bleeding and/or actively bleeding lesion on SBCE was more likely if the procedure was performed while the patient was inpatient (OR=2.051, 95% CI [1.597–2.634; p < 0.0001) (Table 4).

When applying multivariable GEE logistic regression in order to control for the effects of confounding factors, we found that patients being treated with antiplatelet agents and/or anticoagulation were still more likely to have stigmata of recent bleeding or actively bleeding lesion identified on SBCE (OR = 1.507, 95% CI [1.071–2.119]; p = 0.01) (Table 5).

From the 318 patients that had stigmata of recent bleeding or actively bleeding lesions identified on SBCE, 118 (37.1%) had a P1 lesion with intermediate bleeding potential identified on SBCE, 136 (42.8%) had a P2 lesion with high bleeding potential identified (Table 6) [19].

Of the patients that had stigmata of recent bleeding and/or actively bleeding source identified on SBCE, 25.2% (n = 80)underwent subsequent endoscopy. Of these patients 58.8% (n=47) underwent deep (push or device-assisted) enteroscopy, 10% (n=8) underwent enteroscopy and colonoscopy, one patient (1.3%) underwent enteroscopy and EGD, 15% (n=12) underwent an EGD, 6.3% (n=5) underwent a colonoscopy, and 4.8% (n=4) underwent EGD and colonoscopy. From the patients that underwent endoscopy following SBCE, 42 (52.5%) received endoscopic hemostasis therapy, 32 (40%) were started on a PPI (while 37 [46.3%] patients were already on PPI at the time of endoscopy), and one patient was started on octreotide for treatment of recurrent angioectasias. Of the patients that received endoscopic hemostasis therapy, the majority were treated with argon plasma coagulation (APC; n=21 [50%]), the rest were treated with other modalities (3 patients [7.1%] were treated with cautery and clips, 9 [21.4%] with clips alone, 6 [14.3%] with cautery alone, and 3 [7.2%] with APC and clips) (Table 7).

From the patients that had stigmata of recent bleeding and/or actively bleeding source identified on SBCE, 9.8% (n=31) underwent radiologic evaluation. Thirteen (42%) underwent CTA, which was negative. Eleven (35.5%) underwent CTA with embolization. Two patients (6.5%) underwent CTA (which was negative), followed by tagged red blood cells scan. Three patients (9.7%) underwent a

**Table 1** Patient age of those with stigmata of recent and/or actively bleeding lesions identified on SBCE and the those without stigmata of recent and/or actively bleeding lesions identified on SBCE

	Stigmata of Recent and/or Actively Bleeding Lesions Identified on Small Bowel Capsule Endoscopy (Group 1)		No Stigmata of Recent and/or Actively Bleeding Lesions Identified on Small Bowel Capsule Endoscopy (Group 2)			<i>p</i> -value	
	N	$Mean \pm SD$	Range	N	$Mean \pm SD$	Range	
Age	318	$66.97 \pm 14.12$	(14, 90)	1842	$60.21 \pm 17.06$	(10, 93)	<.0001a

<sup>&</sup>lt;sup>a</sup>p-value from independent two samples t-test

**Table 2** Patient characteristics of those with stigmata of recent and/or actively bleeding lesions identified on SBCE and the control patient group

Variable		Group 1	Group 2
		# of obs. (%)	# of obs. (%)
Dialysis	No	200 (93%)	1077 (95.6%)
Requirement	Yes	15 (7%)	50 (4.4%)
Chronic Kidnev	No CKD	31 (23.9%)	128 (27.5%)
Disease (CKD)	Stage 2 CKD	36 (27.7%)	127 (27.3%)
	Stage 3 CKD	40 (30.8%)	124 (26.6%)
	Stage 4 CKD	10 (7.7%)	44 (9.4%)
	Stage 5 CKD	13 (9.9%)	43 (9.2%)
Atrial Fibrillation	No	162 (75.4%)	941 (83.9%)
	Yes	53 (24.6%)	181 (16.1%)
Aortic Stenosis	No	194 (90.7%)	1075 (95.6%)
110. We Stemosis	Yes	20 (9.3%)	50 (4.4%)
Heart Valve	No	204 (93.2%)	1078 (95.7%)
Replacement	Yes	15 (6.8%)	48 (4.3%)
Cirrhosis	No	202 (94%)	1077 (95.2%)
Cirriosis	Yes	13 (6%)	54 (4.8%)
Antiplatelet Agent	No	105 (49.1%)	714 (64.1%)
Innipiaicici Itgeni	Yes	109 (50.1%)	427 (35.9%)
Total Numbers	1	88 (41.1%)	331 (29.7%)
of Antiplatelet	2	21 (9.8%)	69 (6.3%)
Agents	2	21 (7.070)	07 (0.370)
Aspirin	No	111 (52.1%)	752 (68%)
•	Yes	102 (47.9%)	354 (32%)
Clopidogrel	No	185 (87.7%)	1000 (90.1%)
	Yes	26 (12.3%)	110 (9.9%)
Ticagrelor	No	208 (99.3%)	1095 (99.3%)
O .	Yes	2 (0.7%)	8 (0.7%)
Anticoagulation	No	151 (69%)	885 (79.1%)
O	Yes	68 (31%)	234 (20.9%)
Enoxaparin	No	204 (97.1%)	1082 (97.9%)
1	Yes	6 (2.9%)	23 (2.1%)
Warfarin	No	172 (78.9%)	962 (86.3%)
J	Yes	46 (21.1%)	153 (13.7%)
Apixaban	No	201 (95.3%)	1072 (97.1%)
<i>I</i>	Yes	10 (4.7%)	32 (2.9%)
Rivaroxaban	No	201 (96.4%)	1066 (96.4%)
	Yes	9 (3.6%)	40 (3.6%)
Antithrombotic	No Therapy	78 (35.1%)	597 (52.9%)
Therapy	Antiplatelet	111 (50%)	428 (37.9%)
	Agent/s or Anticoagulation (Either one)	()	
	Both Therapies	33 (14.9%)	103 (9.2%)
Patient Status	Outpatient	186 (58.5%)	1369 (74.3%)
	Inpatient	132 (41.5%)	473 (25.7%)

<sup>\*</sup>Values are calculated based on the available data. Some values were not available for all patients

tagged red blood cells scan alone, and one patient (6.3%) underwent a Meckel's scan (Table 7).

Of the patients that had stigmata of recent bleeding and/ or actively bleeding source identified on SBCE, 27.4% (n=87) had recurrent bleeding episodes, and 12.3% (n=38) required hospitalization for this reason. Of the 87 patients who had recurrent episodes of GIB, 11 (29%) had previously undergone endoscopic hemostasis of lesions detected by SBCE prior to the recurrent bleeding episode, and 1 (2.6%) underwent CTA with embolization prior to the recurrent GIB. Twenty-nine patients (9.1%) underwent repeat SBCE as part of the evaluation for recurrent GIB. From the 87 patients that rebled post-SBCE, 28 (32.2%) had a P1 lesion with intermediate bleeding potential identified on their SBCE, 59 (67.8%) had a P2 lesion with high bleeding potential identified on their SBCE [19].

In 2.6% (n=3) of patients taking antiplatelet agents and 23.8% (n=5) of patients taking anticoagulation, these medications were held at least for 1-month post-SBCE. Only one cardiovascular event was documented within 18 months after SBCE, a myocardial infarction at 1-month post-SBCE in a patient whose antiplatelet agent had been discontinued at the time of SBCE.

## **Discussion**

Small bowel bleeding is associated with multiple blood transfusions, prolonged and/or multiple hospital admissions, utilization of significant healthcare resources, and negative effects on patient quality of life [22]. There is a well-recognized association between antithrombotic medications and GIB. Clopidogrel alone and aspirin alone have been shown to increase the risk of upper GIB irrespective of age, gender, comorbidities [23, 24]. Combined antithrombotic treatment confers particular risk, and is associated with high incidence of GIB [25]. In this study we show that antiplatelet agents increased the chance of detecting stigmata of recent bleeding and actively bleeding lesions on SBCE, irrespective of age and comorbidities. These data suggest that SBCE should be part of the routine evaluation of patients presenting with suspected small bowel bleeding who are on antithrombotics and/or hospitalized. In our study we show that by performing inpatient SBCE, we increase the diagnostic yield of SBCE for possible subsequent intervention. Prior studies show that the yield of SBCE increases when performed on hospitalized patients, but this study also suggests increased yield for patients taking antithrombotics. SBCE findings may directly impact the management of these medications in these patients [26].

Prior studies have attempted to identify predictors of positive findings on capsule endoscopy in overt and occult GIB [15–17, 27, 28]. Many of these studies have small sample sizes and limited assessment of demographic and clinical factors. A meta-analysis has shown that antiplatelet or anticoagulant medications led to more overall positive findings on capsule endoscopy [29]. One limitation of



Table 3 Overall yield of small bowel capsule endoscopy (SBCE) and SBCE yield in patients on antiplatelet medications, anticoagulation, and in patients that had their SBCE performed inpatient, and in patients that had their SBCE performed in the outpatient setting

Total Number of Small Bowel Capsule Endoscopy (SBCE) (n = 2160)	Patients with Lesions with Stigmata of Recent or Active Bleeding (n=318)	No Stigmata of Recent or Active Bleeding (n = 1842)	Yield of SBCE
Overall Yield (n)	318	0	14.7%
Antiplatelet Medications (n)	130	472	21.6%
Not on Antiplatelet Medications (n)	188	1558	12.1%
Anticoagulation (n)	68	234	22.5%
Not on Anticoagulation (n)	250	1608	13.5%
Inpatient (n)	132	473	21.8%
Outpatient (n)	186	1369	12%

**Table 4** Results of univariate generalized estimating equation (GEE) logistic regression

Variable	Univariate GEE Logistic Regression [1]			
		OR	95% CI	<i>p</i> -value
Age	$\geq$ 60 years of age vs. $<$ 60	1.025	(1.017, 1.034)	< 0.001
Gender	Male vs. Female	1.165	(0.912, 1.487)	0.2213
Race	White vs. Black	0.721	(0.547, 0.949)	0.0196
Comorbidity	Yes (Y) vs. No (N)	2.141	(1.597, 2.870)	< 0.001
Dialysis	Y vs. N	1.670	(0.913, 3.055)	0.0962
Atrial Fibrillation	Y vs. N	1.686	(1.183, 2.401)	0.0038
Aortic Stenosis	Y vs. N	2.288	(1.326, 3.948)	0.0029
Heart Valve Replacement	Y vs. N	1.683	(0.924, 3.068)	0.0890
Cirrhosis	Y vs. N	1.228	(0.674, 2.237)	0.5021
Antiplatelet Therapy	Y vs. N	2.007	(1.568, 2.569)	< 0.0001
Anticoagulation	Y vs. N	1.703	(1.236, 2.347)	0.0019
Setting	Inpatient vs. Outpatient	2.051	(1.597, 2.634)	< 0.0001

<sup>&</sup>lt;sup>1</sup> Probability model is recent and/or actively bleeding lesions identified on Small Bowel Capsule Endoscopy (SBCE) = Yes.

**Table 5** Results of multivariable generalized estimating equation (GEE) logistic regression

Variable	Variable		Multivariable GEE Logistic		
		Reression [1]			
		OR	95% CI	<i>p</i> -value	
Age	Per year increase	1.006	(0.995, 1.018)	0.2904	
Gender	Male vs. Female	1.113	(0.824, 1.504)	0.4839	
Race	White vs. Black	0.806	(0.577, 1.125)	0.2051	
Therapy	Antiplatelet or Anticoagulation Therapy (Either one) vs. No Therapy	1.507	(1.071, 2.119)	0.0186	
	Both Therapies (Antiplatelet+Anticoagulation) vs. No Therapy	1.516	(0.9365, 2.455)	0.0904	
Setting	Inpatient vs. Outpatient	1.174	(0.794, 1.736)	0.4215	

<sup>1</sup>Probability model is recent and/ or actively bleeding lesions identified on Small Bowel Capsule Endoscopy (SBCE)=Yes

**Table 6** Lesions with stigmata of recent or active bleeding on small bowel capsule endoscopy (SBCE)

Saurin Classification	Small Bowel Capsule	Lesions with Stig-		
	Endoscopy (SBCE)	mata of Recent or		
	Findings	Active Bleeding		
		(n = 318)		
	Non-specific Blood	64 (20.1%)		
P1	Erythema	47 (14.8%)		
	Erosion(s)	71 (22.3%)		
P2	Angioectasia(s)	83 (26.1%)		
	Ulcer(s)	48 (15.1%)		
	Dieulafoy Lesion	4 (1%)		
	Malignancy	1 (0.6%)		

this meta-analysis was the heterogeneity of the studies that were included in the analysis. ESGE recommends continuation of these medications (antithrombotics) before SBCE, because of their association with higher diagnostic rate [18]. We show that the diagnostic yield for detecting stigmata of recent bleeding and/or actively bleeding lesions in SBCE was higher in patients treated with antiplatelet medications and anticoagulation when compared to the patients not being treated with either. Aspirin and thienopyridines can both cause mucosal damage, resulting in erosions and ulcers [30]. Anticoagulation is associated with P2 lesions in the small bowel [31]. In our patient population, angioectasia was the most frequently visualized lesion(s) on SBCE that suggested recent bleeding or active bleeding.



**Table 7** Follow up Data Post-Small Bowel Capsule Endoscopy (SBCE) of the Patients That Had Recent and/or Active Bleeding Identified on SBCE

Variable		n (%)
Endoscopic Procedures	Deep (Push or Device-Assisted) Enteroscopy	47 (58.8%)
Post-Small	Enteroscopy and Colonoscopy	8 (10%)
Bowel Cap- sule Endos-	Enteroscopy and Esophagogastroduo- denoscopy (EGD)	1 (1.3%)
copy (SBCE) $(n=80)$	EGD	12 (15%)
(n=80)	Colonoscopy	5 (6.3%)
	EGD and Colonoscopy	4 (4.8%)
Therapeutic	None	38 (47.5%)
Intervention	Performed	42 (52.5%)
Therapeutic	Argon Plasma Coagulation (APC)	21 (50%)
Intervention	Cautery + Clips	3 (7.1%)
	Clips	9 (21.4%)
	Cautery	6 (14.3%)
	APC+Clips	3 (7.2%)
Radiologic Evaluation	Computed Tomography Angiography (CTA)	13 (42%)
	CTA with Embolization	11 (35.5%)
	CTA and Tagged Red Blood Cells Scan	2 (6.5%)
	Tagged Red Blood Cells Scan	3 (9.7%)
	Meckel's Scan	1 (6.3%)

This is the first study to report how SBCE findings influenced subsequent care. Positive SBCE findings led to repeat endoscopy, with the majority undergoing deep enteroscopy. We also show that half of the patients who underwent subsequent endoscopy received endoscopic hemostasis, with the majority of them having angioectasia treated by APC. Positive findings in SBCE also led to radiographic evaluation and intravascular embolization. Similar to prior studies, we show that approximately a quarter of patients with positive SBCE findings have recurrent GIB. We additionally show that the majority of these patients had a P2 lesion on SBCE, and approximately half of these patients required hospitalization for the episode of recurrent GIB [32].

Although this is a retrospective, single-center study, it has the merit of being one of the largest known cohorts comparing SBCE yield in patients taking antithrombotic therapy in the inpatient vs. outpatient setting. All SBCEs in this study were interpreted by a single gastroenterologist with considerable expertise in the field. Any potential biases or idiosyncrasies in interpretation, therefore, should be evenly distributed among the cohorts.

This study also has limitations. Not all information was available for all patients that underwent SBCE. All SBCE were performed and interpreted in a tertiary center with considerable expertise in complex GIB and capsule endoscopy, which may not be broadly applicable.

Finally, our study emphasizes the high value yield of SBCE as part of the evaluation for suspected small bowel bleeding in those patients with unrevealing bi-directional endoscopy, particularly in hospitalized patients and those taking antithrombotic therapy. The analysis of post-SBCE care illustrates how positive SBCE findings influence subsequent management of GIB.

**Author contributions** S.D., D.K, and A.C., collected the data. S.D., S.M, and P.F performed the analysis and prepared all the figures. S.D. wrote the main text. D.K. and G.I. edited the main text and provided mentorship. All authors reviewed the manuscript.

**Data availability** All data supporting the findings of this study are available within the paper.

## **Declarations**

**Competing interests** The authors declare no competing interests.

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