Minimally-invasive imaging of the small intestine

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Chapter 7

Video capsule endoscopy for previous overt obscure gastrointestinal bleeding in patients using anti-thrombotic drugs

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Summary

Background and Aims

Little is known on the causes of overt obscure gastrointestinal bleeding (OGIB) in patients using anti-thrombotic therapy. We aimed to describe video capsule endoscopy (VCE) findings and to identify factors associated with positive findings in these patients.

Methods

We carried out a retrospective study of 56 patients who underwent VCE for evaluation of previous overt OGIB during anti-thrombotic therapy. VCE examinations were re-evaluated by a gastroenterologist blinded to clinical details. Clinical data included in the multivariate analysis were: sex, age, indication for and type of anti-thrombotic therapy, haemodynamic instability on admission, type of blood loss, haemoglobin on admission, use of a proton pump inhibitor, non-steroidal anti-inflammatory drug use, time between bleeding episode and VCE, and whether or not anti-thrombotic therapy was resumed before the VCE examination.

Results

A probable cause for gastrointestinal bleeding was identified in 28 (50%) of the 56 studies. Angioectasia were found in 19 patients. Twenty-two studies showed a possible cause in the small bowel. Multivariate logistic regression analysis showed that reinstitution of anti-thrombotic therapy before VCE was carried out was the only independent predictor of positive VCE findings (OR 8.61; 95% CI, 1.20–60.42; $p = 0.032$).

Conclusions

Small-intestinal angioectasia were the most common cause for overt OGIB. Reinstitution of withdrawn anti-thrombotic drugs before the VCE examination was carried out, was associated with positive VCE findings in multivariate analysis.

Introduction

Acute gastrointestinal bleeding has been reported in up to 12% of patients on anti-thrombotic therapy.[1-4] Oral anti-thrombotic therapy might cause gastrointestinal bleeding by inducing mucosal damage (aspirin), impairing mucosal healing (aspirin and thienopyridines), or by aggravating blood loss from pre-existing lesions (coumarins, aspirin and probably thienopyridines).[5] A study on almost three thousand patients showed the age-adjusted relative risk for major upper gastrointestinal bleeding to be 4.0 for aspirin-users and 2.3 for thienopyridines-users, whereas a different group found the relative risk for major gastrointestinal bleeding to be 7.1 for coumarin users.[6, 7] It has been estimated that antiplatelet drugs are associated with up to 14.5% of all cases of upper gastrointestinal bleeding, whereas coumarin therapy has been connected with up to 25% of all acute gastrointestinal bleeding episodes.[6, 7]

In patients with acute gastrointestinal blood loss while on oral anti-thrombotic therapy, urgent endoscopic evaluation is advised, as 30–50% will have peptic ulcer bleeding requiring endoscopic therapy.[8, 9] The decision to reverse anti-thrombotic agents should be made after the risk of thromboembolic complications has been weighed against the risk of continued bleeding.[10, 11] After appropriate endoscopic management, it is generally considered safe to reinstitute anti-thrombotic therapy after a few days.[10, 11]

In approximately 5% of patients presenting with acute gastrointestinal haemorrhage, no source can be found by upper endoscopy and colonoscopy.[12] Additionally, in approximately 75% of these cases of overt obscure gastrointestinal bleeding (OGIB) a cause is found in the small bowel.[12] A recent study found a small-intestinal bleeding locus in 1.2% of patients with overt gastrointestinal bleeding.[13] Patients with acute overt OGIB have worse outcomes compared to patients with acute colonic or upper GI bleeding and require a higher number of diagnostic procedures.[14] Although the diagnostic yield of VCE in patients with overt OGIB has been reported to be 64–92%, no specific data on patients using anti-thrombotic agents have been published.[15-17]

In one study carried out before video capsule endoscopy (VCE) or balloon assisted enteroscopy were available, nine of 52 anticoagulated patients with severe gastrointestinal haemorrhage had a normal oesophagogastroduodenoscopy and colonoscopy.[8] There are no data on when or how to reinstitute oral anti-thrombotic therapy in the absence of an identified cause.

Aim of our study was to assess the diagnostic yield of VCE in patients with previous overt OGIB while on oral anti-thrombotic therapy, to describe VCE-findings and to identify factors associated with positive findings of VCE.

Patients and methods

Patients

We carried out a retrospective review of all patients undergoing VCE from December 2003 to September 2008 at VU University Medical Centre. All patients or their legal

representatives had given informed consent for the VCE examination. This retrospective study was approved by our institutional review board. The requirement for informed consent was waived. Our centre is a tertiary referral clinic for small bowel disease. A total of 904 VCE examinations were carried out during the study period. Of these, 111 patients had an episode with acute melaena and/or haematochezia requiring hospitalization, without an identified bleeding source at conventional endoscopy. These patients were considered to have had overt OGIB and were considered eligible for inclusion.[14] Of these examinations, 56 (50.5%) were performed in patients who used oral anti-thrombotic therapy (coumarins, aspirin and/or thienopyridines) at the time of the bleeding episode. Only these VCE examinations were included in this analysis.

VCE was performed after medical records were reviewed by one of two gastroenterologists (S. V. W. and M. J.) experienced in VCE, to assess possible contraindications for VCE, such as symptoms suggestive of small bowel obstruction. If symptoms of small bowel obstruction were present, radiological small-bowel imaging was recommended or emergency double-balloon endoscopy (DBE) was offered. In cases of life-threatening ongoing overt OGIB, emergency DBE was offered.

The decision to continue or withdraw oral anti-thrombotic therapy during admission, as well as whether or not to reinstitute these drugs after the bleeding episode, was made by the referring physician. These decisions were made after assessment of the severity of the bleeding episode, the estimated risk of rebleeding (taking into account that, by definition, no cause had been found during routine gastrointestinal examinations) and the estimated risk of thromboembolic events. Such an individualized approach is recommended in recent guidelines.[10]

Clinical data collected were: age and sex, whether or not the patient was referred, indication for oral anti-thrombotic therapy, haemodynamic instability on admission (defined as a pulse ≥ 100 beats per minute or systolic blood pressure < 100 mm Hg), type of blood loss (melaena, haematochezia or both), haemoglobin count on admission, type of anti-thrombotic drug (acenocoumarol, aspirin or clopidogrel, or any combination therapy), concurrent use of a proton pump inhibitor (PPI), time between bleeding episodes and VCE, and use of anti-thrombotic therapy at the time of VCE examination. The international normalized ratio (INR) at the time of bleeding or at the time of the VCE examination were not measured in all patients, and therefore not included in this analysis.

Video capsule endoscopy protocol

The Pill Cam SB capsule endoscope (Given imaging, Yoqneam, Israel) was used for 879 (97.1%) of the VCE examinations. For 26 (2.9%) VCE examinations the Mirocam (Intromedic, Seoul, Korea) was used. Patient preparation consisted of 2 litres of polyethylene glycol bowel preparation (Klean prep, Norgine, Amsterdam, The Netherlands) at midday 1 day before the examination and nil by mouth after midnight before the examination. Patients were allowed liquids 4 hours after ingestion of the capsule and solid food after 8 hours. We used this protocol since VCE is being carried out in our centre.[18]

All included VCE examinations were re-evaluated by one gastroenterologist (S.V.W.) with over 5 years experience in VCE and who was blinded to the clinical data during the capsule reading sessions. Positive findings were categorised in three categories, modified from the original classification by Saurin and co-workers:[19]

- Actively bleeding lesions or lesions with a high potential for bleeding based on size and/or number (P2); e.g.: multiple or bleeding angioectasia;
- Smaller and/or less numerous lesions with an intermediate potential for bleeding (P1); e.g.: isolated non-bleeding angioectasia;
- Lesions without any disruption of the mucosa and no potential for bleeding (P0); e.g.: red spots.

A positive VCE diagnosis was defined as the presence of one or more P2 and/or P1 lesions. A negative VCE diagnosis was defined as the presence of one or more P0 lesions in the absence of P1 or P2 lesions, or as the absence of any abnormality. Additional data collected included the location of abnormalities depicted (small bowel, stomach, colon), type of abnormalities depicted and whether the capsule had reached the caecum within battery lifetime.

Statistical analysis

We performed comparisons between variables using Student's *t* test for continuous variables and Fisher's exact test or the two-sided χ^2 test for categorical variables. The relationship between positive findings and the interval between the bleeding episode and VCE was explored by calculation of the area under the receiver operating characteristic curve, assuming that a shorter interval could be associated with positive findings. Factors independently associated with positive findings at VCE were investigated using stepwise logistic regression analysis using the following parameters: sex, age, indication for anti-thrombotic therapy (atrial fibrillation, coronary artery disease, arterial embolic disease, other), haemoglobin on admission, haemodynamic instability, type of blood loss (melaena, haematochezia, mixed), time between bleeding episode and VCE, PPI use, NSAID use, type of anti-thrombotic drug used (acenocoumarol, aspirin or clopidogrel, any combination) and use of anti-thrombotic drug during VCE. *P* values < 0.05 were considered to indicate statistical significance.

Results

Details of the 56 patients included in this analysis, as well as the results of VCE are shown in ***table 7.1***. All patients had undergone at least one complete oesophagogastroduodenoscopy and complete ileocolonoscopy within 3 days after admission. Oral anti-thrombotic therapy had been withheld after the initial bleeding episode in all patients for at least 3 days, and was reinstituted in 25 (44.6%) patients, all within 10 days after the bleeding episode. The mean time (± SD) between reinstitution of anti-thrombotic drugs and capsule endoscopy was 29 (± 29) days. The mean time between the bleeding episode and

Table 7.1: Characteristics of the patient population and procedural details and diagnostic yield of video capsule endoscopy.

Parameter	Result
Male gender	40 (71)
Age (mean ± standard deviation, range)	72 ± 12 (25–87)
Referred from other hospital	44 (79)
Type of oral anti-thrombotic therapy	
Acenocoumarol	26 (46)
Aspirin alone	20 (36)
Clopidogrel alone	2 (4)
Acenocoumarol and aspirin	4 (7)
Acenocoumarol and clopidogrel	0 (0)
Aspirin and clopidogrel	3 (5)
Acenocoumarol, aspirin and clopidogrel	1 (2)
Indication for oral anti-thrombotic therapy	
Atrial fibrillation	13 (23)
Coronary artery disease (PTCA with or without stent, n = 6; CABG, n = 7; Other coronary artery disease, n = 2)	15 (27)
Arterial embolic disease (CVA or TIA, n = 9; retinal occlusion, n = 1)	10 (18)
Other (valvular disease, n = 7; Cardiomyopathy, n = 1; vascular endoprothesis, n = 3; pulmonary embolism or recurrent DVT, n = 4; combination, n = 2; unknown, n = 1)	18 (32)
Proton pump inhibitor	23 (41)
Type of blood loss	
Melaena	37 (66)
Haematochezia	9 (16)
Mixed	10 (18)
Haemoglobin on admission (mmol/L ± standard deviation, range)	5.2 ± 1.2 (3.0–8.4)
Haemodynamic instable	8 (14)
Anti-thrombotic therapy at time of VCE	
Reinstituted	25 (45)
Still withheld	31 (55)
Median time between bleeding episode and VCE (days, range)	29 (1–151)
Caecum reached during battery lifetime	50 (89)
VCE-findings	
No abnormalities	17 (30)
P0	11 (20)
P1	16 (29)
P2	12 (21)

Table 7.1: Continued

Parameter	Result
Details of positive VCE findings (***n***, % of positive VCE examinations)	
Small intestine (n = 22)	
Angioectasia (multiple or bleeding)	8 (29)
Angioectasia (isolated and not bleeding)	9 (32)
Tumour	1 (4)
Portal hypertensive enteropathy	1 (4)
Ulcerative stenosis	2 (7)
Dieulafoy's lesion	1 (4)
Stomach and bulb (n = 2)	
Ulcer	2 (7)
Colon (n = 4)	
Angioectasia (multiple or bleeding)	2 (7)
Active bleeding without a clear lesion	2 (7)

Note: Unless otherwise indicated, numbers indicate number of patients, with percentages between parentheses. PTCA = Percutaneous transluminal coronary angioplasty; CABG = coronary artery bypass graft; DVT = deep venous thrombosis; CVA = cerebrovascular accident; TIA = transient ischaemic attack; VCE = video capsule endoscopy.

VCE was 29 days. No adverse events related to the VCE examinations occurred. The relation between positive findings and the interval between the bleeding episode and the VCE-examination was investigated using receiver operating characteristic analysis. The area under the receiver operating characteristic curve was 0.53, indicating no statistically significant relationship between these variables.

A bleeding source was identified by VCE in 28 (50.0%) of the 56 patients. Twenty-two of the 28 positive studies showed a possible cause in the small bowel (***figure 7.1***), whereas two studies showed lesions in the stomach or duodenal bulb and four studies showed lesions or active bleeding in the colon (***figure 7.2***). None of the bleeding sources detected by VCE in the stomach or colon were identified during the initial endoscopic evaluations. However, fresh blood was seen in the colon during initial colonoscopy in all four patients in whom VCE identified a colonic bleeding source.

Nineteen of the 28 positive VCE-studies showed angioectasia in either the small bowel (n = 17) or caecum (n = 2). Both small-bowel stenoses were benign. One was probably NSAID-related, whereas the other was probably of ischemic origin. Active bleeding lesions were found in seven patients and included two cases of small-intestinal angioectasia, one case of small-intestinal stenosis (***figure 7.3***), one case of gastrointestinal stromal cell tumour (***figure 7.4***), and in three cases without a clear origin. One of these cases proved to be a gastric ulcer, one case colonic diverticular bleeding and one bleeding from prolapsed redundant colonic folds.

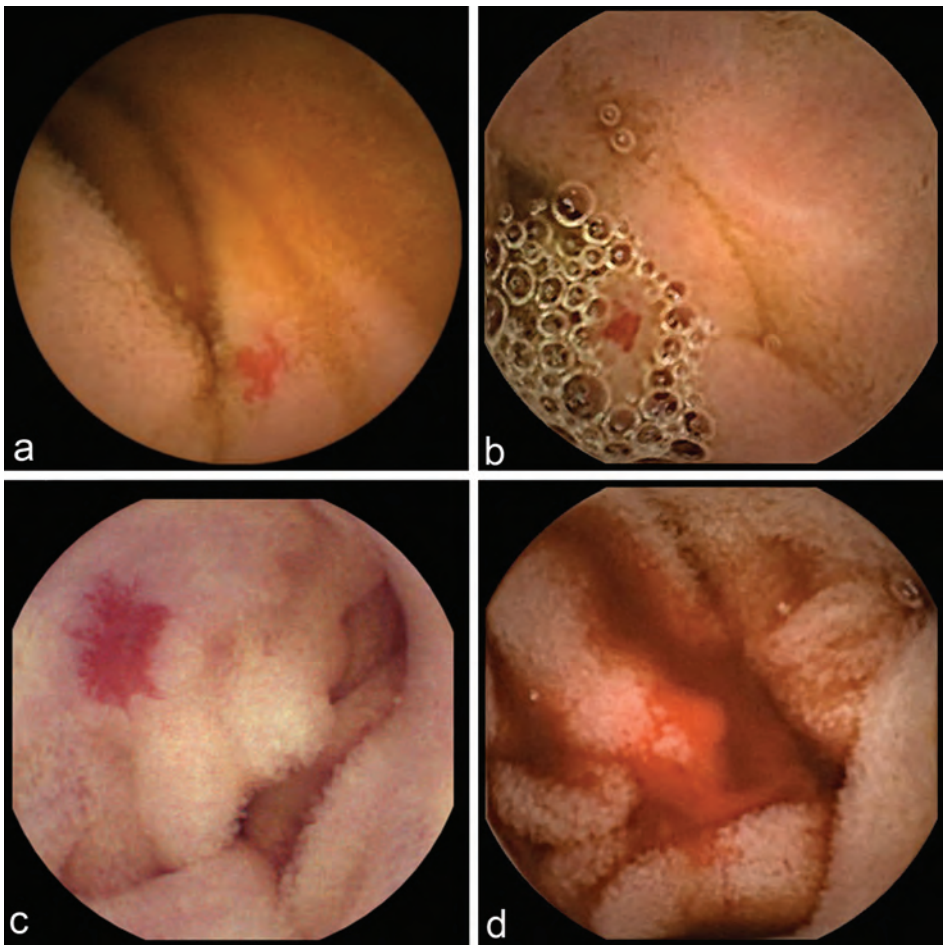

Figure 7.1: Examples of positive VCE findings in the small intestine. (a) Small isolated jejunal angioectasia (P1-type lesion) in a 69-year-old man. (b) Small ileal isolated angioectasia (P1-type lesion) in a 71-year-old man. (c) Large isolated jejunal angioectasia (P2-type lesion) in an 85-year-old man. (d) Active bleeding Dieulafoy lesion (P2-type lesion) in the jejunum of a 77-year old-woman.

The use of anti-thrombotic therapy at the time of the VCE examination was the only factor that differed significantly between patients with negative and positive VCE findings in multivariate analysis (***table 7.2***). Although anti-thrombotic therapy had more frequently been reinstituted in patients with valvular disease or neurological conditions, there was no clear statistical relationship between the indication for anti-thrombotic drug use and whether or not this therapy had been reinstituted (***table 7.3***). The yield of VCE in patients who were on anti-thrombotic therapy during VCE was 80.0%, whereas the yield of VCE in patients in whom anti-thrombotic therapy had not been reinstituted was 25.8%. The association between capsule-endoscopy-findings and kind of anti-thrombotic therapy is shown in ***table 7.4***.

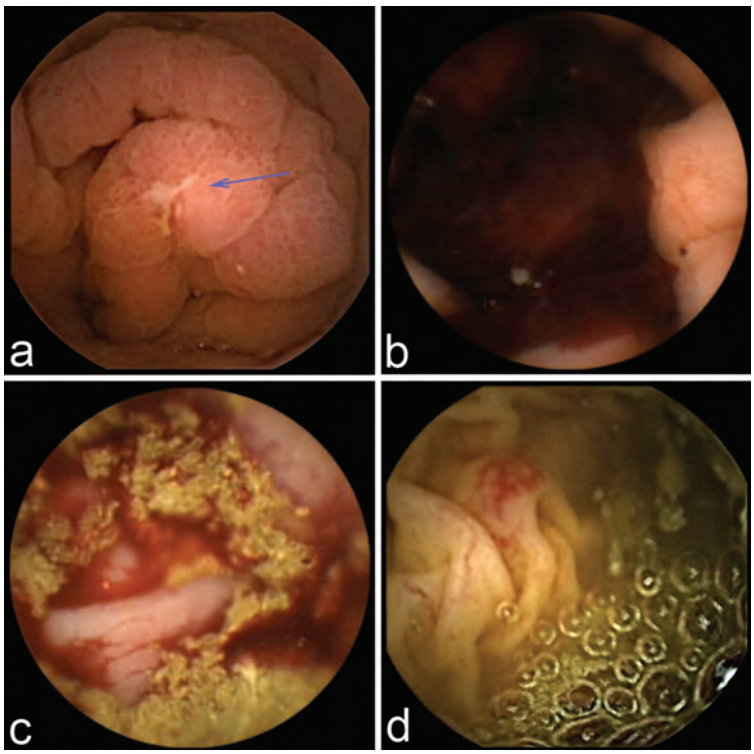

Figure 7.2: Examples of positive VCE findings in the stomach, duodenal bulb and colon. (a) Video capsule image shows a clean based ulcer (arrow) in the duodenal bulb of a 67-year-old man. (b) Large intragastric blood clot and fresh blood in a 79-year-old male patient using acenocoumarol during capsule endoscopy. Upper endoscopy after video capsule endoscopy revealed a small ulcer with visible vessel that was not identified during initial upper endoscopy. (c) Blood in the sigmoid of an 89-year-old woman. Repeated colonoscopy revealed prolapsed redundant folds. (d) Solitary large angioectasia (P2-type lesion) in the colon of a 77-year-old man.

Discussion

In this retrospective study of 56 patients who underwent VCE because of previous overt OGIB while on anti-thrombotic therapy, the overall diagnostic yield was 50%. Small-intestinal angioectasia was the most commonly identified cause. The use of anti-thrombotic drugs during VCE examination was the only factor independently associated with positive VCE findings.

We investigated this very specific group of patients with overt OGIB, so our results cannot be applied to patients with occult OGIB. Acute small-bowel bleeding is a distinct clinical entity requiring a different approach than small-bowel blood loss without signs of overt bleeding.[14]

The diagnostic yield of VCE in our group is comparable to the 53% yield Esaki and co-workers found in a group of 68 patients (17 with anti-thrombotic therapy) with overt

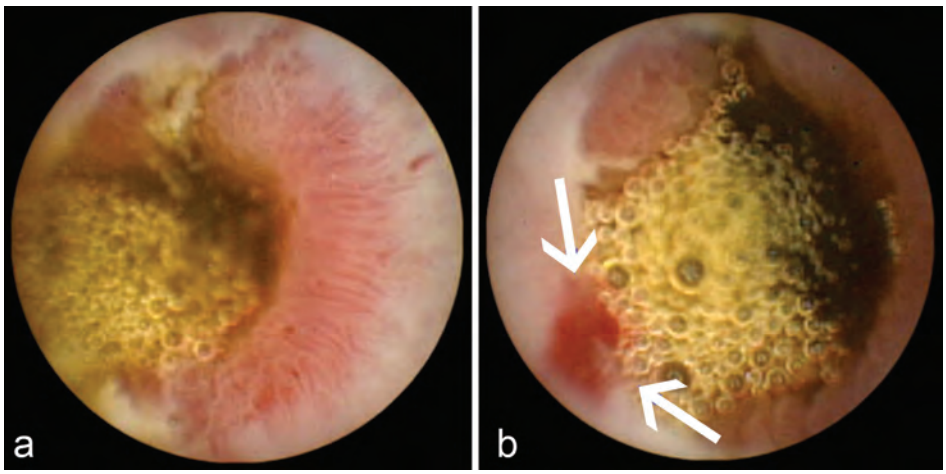

Figure 7.3: Seventy-seven-year-old man with melaena. (a) Video capsule image shows a NSAID-related stenosis in the mid-jejunum. (b) After several minutes capsule-induced bleeding was observed.

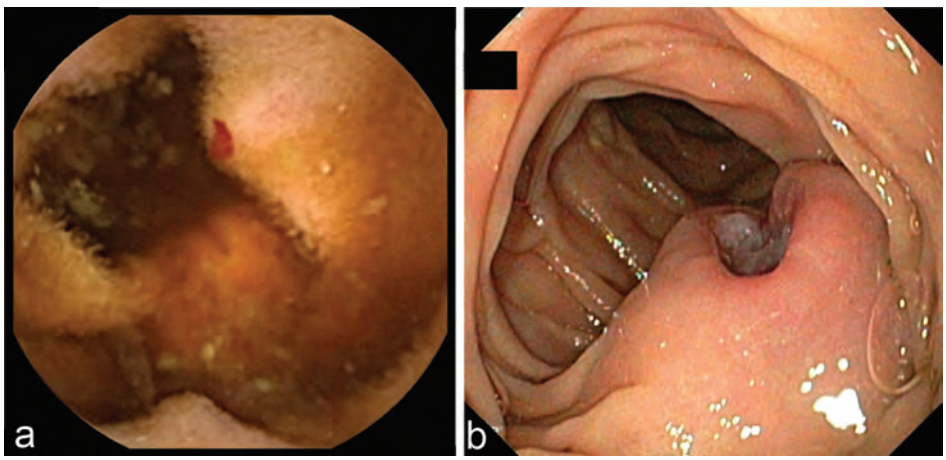

Figure 7.4: Seventy-nine year-old male patient with melaena. (a) Video capsule image shows active bleeding in the proximal jejunum. A mass is present in the middle of the image. (b) Double-balloon endoscopy depicted a 4 cm large tumour with central ulceration. Histopathologic analysis of biopsy specimens showed this lesion to be a gastrointestinal stromal cell tumour.

OGIB.[20] A study on 37 patients with overt OGIB showed that VCE, when carried out within the first 48 hours of the bleeding episode, revealed a definitive source of bleeding in 62% of patients.[15] As in our study, the majority of bleeding sources were angioectasia. The high prevalence of angioectasia as the cause of overt OGIB has also been confirmed in a study on 44 patients with overt OGIB: of the 28 examinations with positive and uncertain findings, angioectasia were recognized in 19.[17]

Table 7.2: Multivariate analysis of risk factors for positive video capsule endoscopy findings.

Parameter	Video capsule endoscopy findings		Odd's ratio (95% CI)	*P* value
	Negative	Positive		
Gender				0.693
Female	8 (29)	8 (29)	1	
Male	20 (71)	20 (71)	0.67 (0.09–4.82)	
Age in years (mean ± SD)	70.2 ± 13.6	74.1 ± 8.9	1.05 (0.99–1.11)	0.056
Indication for anti-thrombotic therapy				
Atrial fibrillation	10 (36)	3 (11)	1	0.373
Coronary artery disease	7 (25)	8 (29)	7.11 (0.33–152.60)	0.210
Arterial embolic disease	3 (11)	7 (25)	31.98 (0.52–1983.47)	0.100
Other	8 (29)	10 (36)	4.44 (0.61–90.15)	0.115
Hb (mmol/L) on admission (mean ± SD)	5.4 ± 1.3	5.0 ± 1.1	0.67 (0.33–1.36)	0.266
Haemodynamic instability				0.266
No	25 (89)	23 (82)	1	
Yes	3 (11)	5 (18)	1.32 (0.07–25.25)	
Type of blood loss				
Melaena	16 (57)	21 (75)	1	0.314
Haematochezia	5 (18)	4 (14)	0.62 (0.07–5.79)	0.674
Mixed	7 (25)	3 (11)	0.12 (0.01–1.92)	0.132
Time between admission and VCE (days ± SD)	29 ± 22	29 ± 29	0.99 (0.96–1.03)	0.687
NSAID use				0.484
No	27 (96)	25 (89)	1	
Yes	1 (4)	3 (11)	6.06 (0.04–941.27)	
Proton pump inhibitor use				0.087
No	20 (71)	13 (46)	1	
Yes	8 (29)	15 (54)	6.87 (0.76–62.19)	
Type of anti-thrombotic therapy				
Acenocoumarol	13 (46)	13 (46)	1	0.208
Antiplatelet monotherapy	13 (46)	9 (32)	0.20 (0.02–2.66)	0.224
Any combination (anticoagulation & anti-platelet)	2 (7)	6 (21)	3.26 (0.14–74.96)	0.459
Anti-thrombotic therapy at time of VCE				0.032
Still withheld	23 (82)	8 (29)	1	
Reinstituted	5 (18)	20 (71)	8.61 (1.20–60.42)	

Note: Unless otherwise indicated, numbers indicate number of patients, with percentages between parentheses. VCE = video capsule endoscopy; CI = confidence interval; Hb = haemoglobin; NSAID = non-steroidal anti-inflammatory drug.

Table 7.3: Indication for anti-thrombotic therapy for patients in whom the anti-thrombotic therapy was either reinstituted or still withheld at time of video capsule endoscopy.

Parameter	Anti-thrombotic drug reinstituted (*n* = 25)	Anti-thrombotic drug withheld (*n* = 31)
Atrial fibrillation	4 (16)	9 (29)
Percutaneous transluminal coronary angioplasty with or without stent	4 (16)	2 (19)
coronary artery bypass graft	2 (8)	5 (16)
Other coronary artery disease	0 (0)	2 (6)
Valvular disease	5 (20)	2 (6)
Cardiomyopathy	1 (4)	0 (0)
Vascular endoprothesis	1 (4)	2 (6)
Pulmonary embolism or recurrent deep venous thrombosis	2 (8)	2 (6)
Cerebrovascular accident or transient ischaemic attack	6 (24)	3 (10)
Retinal occlusion	0 (0)	1 (3)
Combination	0 (0)	2 (6)
Unknown	0 (0)	1 (3)

Note: Numbers indicate number of patients, with percentages between parentheses.

In six of the 28 VCE examinations that revealed a bleeding source, this source was within the reach of conventional endoscopy. VCE studies revealing significant lesions in the stomach and the colon have been reported previously. Peter and co-workers described significant gastric lesions in 12% of patients undergoing VCE, whereas Kitiyakara and Selby identified from a database of 140 patients four patients with significant gastric lesions and five patients with significant colorectal lesions, including two patients with carcinoma.[21, 22]

There are two possible explanations for our observation that reinstitution of anti-thrombotic drugs was associated with an increased yield of VCE. First, it may be possible that with withdrawal of anti-thrombotic drugs, the lesions responsible for the bleeding episode had healed and therefore were no longer present at the time of VCE. This may be especially true for small bowel erosions or ulcers, which are associated with the use of both aspirin and thienopyridines.[5] If this were the case, we would have expected to find small-bowel erosions or ulcers in patients who had continued aspirin or thienopyridines, which in fact, we did not. A more likely cause for our findings may be that in patients who use anti-thrombotic therapy at the time of VCE, pre-existing lesions are more clearly visible because of signs of active or recent blood loss. This would explain why 12 of the 28 positive VCE studies occurred in patients who had continued the use of coumarins alone, which is not known to cause small-bowel lesions. Additionally, the fact that only 4 of the 28 lesions found (ulcers, $n = 2$; ulcerative stenosis, $n = 2$) could possibly have been caused by aspirin or thienopyridines, suggests aggravation of blood loss from pre-existing mucosal disease to be the most important factor in overt OGIB associated with anti-thrombotic drugs in our population.

Table 7.4: Video capsule findings according to type of anti-thrombotic drug reinstituted or still withheld.

	Anti-thrombotic therapy reinstituted (*n* = 25)	Anti-thrombotic therapy withheld (*n* = 31)
Acenocoumarol alone (*n* = 26)		
No abnormalities or P0 lesions	2	11
Small bowel findings		
Angioectasia (multiple or bleeding)	5	1
Angioectasia (isolated and not bleeding)	3	—
Portal hypertensive enteropathy	1	—
Ulcerative stenosis	2	—
Stomach and bulb findings		
Ulcer	1	—
Antiplatelet (aspirin or clopidogrel) monotherapy (*n* = 22)		
No abnormalities or P0 lesions	2	11
Small bowel findings		
Angioectasia (multiple or bleeding)	2	3
Angioectasia (isolated and not bleeding)	1	—
Tumour	—	1
Stomach and bulb findings		
Ulcer	—	1
Colon findings		
Angioectasia (multiple or bleeding)	1	—
Active bleeding, no clear lesion	—	1
Any combination (*n* = 8)		
No abnormalities or P0 lesions	1	1
Small bowel findings		
Angioectasia (multiple or bleeding)	2	1
Dieulafoy's lesion (bleeding)	1	—
Colon findings		
Angioectasia (multiple or bleeding)	1	—
Active bleeding, no clear lesion	1	—

Note: numbers indicate number of patients.

The observation that anti-thrombotic therapy might be able to reveal sites of gastrointestinal bleeding that remained obscure while coagulation was not impaired, is not new. The deliberate use of anti-thrombotic therapy during endoscopy to provoke gastrointestinal bleeding in order to find a source for OGIB has been described in several case reports.[23-25] Additionally, tissue plasminogen activator and heparin have been

successfully used to provoke gastrointestinal bleeding during angiography in larger series of patients with recurrent OGIB.[26, 27]

The retrospective nature of our study and the limited number of patients included, limit the generalizability of our study. As no standard method of endoscopic follow-up of all positive and negative findings was performed, we do not know whether or not the yield of VCE represents only true positive findings. We could not investigate the possible association between yield and INR values because these were not routinely measured during VCE. We therefore do not know whether or not over-anticoagulation had an influence on the capsule findings.

Recent investigations have indicated that the yield of VCE in patients with OGIB is higher when VCE is performed within 1 or 2 weeks after the bleeding episode.[15, 20, 28, 29] This was not confirmed in our study, which might be explained by the long interval between the bleeding episodes and the VCE examinations. This is probably the result of the referral character of our centre. An additional factor could be our policy to perform emergency DBE rather than VCE in patients with life-threatening ongoing overt OGIB.[30]

One might argue that if no lesions are found after withdrawal of the offending anti-thrombotic drug, the bleeding problem is solved. However, in patients who use anti-thrombotic therapy for clearly established indications, withdrawal of these drugs imposes an increased risk of thromboembolic events.[31] A recent report showed that discontinuation of antiplatelet agents in patients with endoscopically treated upper gastrointestinal bleeding was associated with increased (cardiovascular) mortality.[32]

Our study was not aimed to investigate the benefits or disadvantages of continuation of anti-thrombotic therapy. Therefore we did not include the occurrence of thromboembolic events in our study. Apart from this, we do not believe that routine continuation of anti-thrombotic drugs should be advocated in every patient with gastrointestinal bleeding before endoscopic treatment has been performed, let alone in patients in whom no bleeding locus has been identified, as was the case for all patients included in our study. Decisions to do so should always be based on careful consideration of both the bleeding risk associated with continuation of anti-thrombotic drugs as well as the cardiovascular risks of withdrawal of such agents.[10, 11]

A relation between yield and continuation of oral anti-thrombotic drugs might also exist for other endoscopic modalities used to evaluate gastrointestinal bleeding. In many centres anti-thrombotic drugs are discontinued 1 week before endoscopy. If this is also the case for enteroscopy this might explain why positive VCE findings often cannot be confirmed with device assisted enteroscopy. This might, for instance, clarify why positive VCE-findings frequently cannot be confirmed with DBE.[33]

In summary, in our population with previous overt OGIB while on anti-thrombotic therapy, small-intestinal angioectasia were the most common cause. The use of anti-thrombotic drugs, at the time of VCE was associated with an increased yield. Further prospective studies are needed to determine the clinical relevance of our findings, both in patients with overt, as in patients with occult, OGIB.

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