

Scoring systems in clinical small-bowel capsule endoscopy: all you need to know!



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ABSTRACT

Capsule endoscopy (CE) emerged out of the pressing clinical need to image the small bowel (SB) in cases of midgut bleeding and provide an overall comfortable and reliable gastrointestinal (GI) diagnosis [1]. Since its wider adoption in clinical practice, significant progress has been made in several areas including software development, hardware features and clinical indications, while innovative applications of CE never cease to appear [2, 3]. Currently, several manufacturers provide endoscopic capsules with more or less similar technological features [4]. Although there is engaging and continuous academic and industry-fueled R&D, promising furtherment of CE technology [4, 5], the current status of clinical CE remains that of by and large an imaging modality. Clinical relevance of CE images is cornerstone in the decision-making process for medical management. In one of the larger to date SB CE studies, 4,206 abnormal images were detected in 3,280 patients [6]. Thus, CE leads to the identification of a large amount of potential pathology, some of which are pertinent (or relevant) while some (probably the majority) are not. Soon artificial intelligence (AI) is likely to carry out several roles currently performed by humans; in fact, we are witnessing only the first stages of a transition in the clinical adoption of AI-based solutions in several aspects of gastroenterology including CE [7]. Until then though, human-

based decision-making profoundly impacts patient care and – although not suggested in the updated European Society of Gastrointestinal Endoscopy (ESGE) European curriculum [8, 9] – it should be an integral part of CE training. Frequently, interpretation of CE images by experts or at least experienced readers differs. In a tandem CE reading study, expert review of discordant cases revealed a 50% (13/25 discordant results) error rate by experienced readers, corresponding (in 5/13 cases) to ‘over-classification’ of an irrelevant abnormality [10]. Another comparative study showed an ‘over-classification’ of such irrelevant abnormalities in ~10% of CE readings [11]. One thing which has been for a while on the table – in relation to optimizing and/or standardizing CE reporting and subsequent decision-making – is the need for reproducible scoring systems and for a reliable common language among clinicians responsible for further patient’s management.

Over the years, several of these scoring systems were developed while others appear in the wake of software and hard-

ware improvements aiming to replace and/or complement their predecessors. This review presents a comprehensive account of the currently available classification/scoring systems in clinical CE spanning from predicting the bleeding potential of identified SB lesions (with emphasis on vascular lesions), and the individual rebleeding risk; scoring systems for the prediction of SB lesions in patients with obscure gastrointestinal bleeding (OGIB), having the potential to improve patient selection and rationalize the use of enteroscopy, with better allocation of resources, optimized diagnostic workflow and tailored treatment. This review also includes scores for reporting the inflammatory burden, the cleansing level that underscores confidence in CE reporting and the mass or bulge question in CE. Essentially, the aim is to become a main text for reference when scoring is required and facilitate the inclusion of -through readiness of access- one of the other in the final report.

Nomenclature & classification of SB lesions with bleeding potential

The diagnosis and interpretation of SB vascular lesions is not always straightforward. Therefore, the use of a common terminology and standardized classification system to describe the probability of haemorrhagic lesions in the SB is essential to improve our knowledge of the natural history, expected outcomes and optimize management of patients with midgut bleeding (MGB). A consensus statement on the nomenclature and semantic description of vascular lesions in small-bowel capsule endoscopy (SBCE) was recently established [12], aiming to improve standardization of reading, teaching, and medical research on this topic, ► **Table 1**. A similar methodology has been followed to standardize terminology of ulcerative and inflammatory lesions in CD [13], ► **Table 2**.

MGB refers to SB bleeding originating distal to the ampulla of Vater and proximal to the ileocecal valve (ICV) [14]. It accounts for most cases of obscure GI bleeding (OGIB), representing 5% to 10% of all cases of GI bleeding, and it presents clinically as occult (positive fecal occult blood tests and/or iron deficiency anemia [IDA]) or overt (melena or hematochezia) bleeding [14, 15]. In a large systematic review of 227 SBCE studies, the CE detection rate of a causative factor in OGIB was 58.6%, with >50% of patients having angiectasias, followed by inflammatory lesions (26.8%) and tumors (8.8%) [16]. Admittedly, angiectasias are the most common source of OGIB in patients older than 60 years, while patients <40 years are more likely to have CD, Meckel’s diverticula, and SB tumors [17, 18].

CE detects a lot of abnormal and/or unusual images in the SB; its limitation, therefore, is not sensitivity but specificity, and recognizing the relevance of any ‘abnormal’ images in the causation of MGB episodes. Based on our experience in therapeutic enteroscopy, the main risk for patients is – in fact – un-

necessary enteroscopy prompted by overinterpretation of CE findings. Our practice is to reject at least one in three therapeutic enteroscopy requests after reviewing CE findings (unpublished data). In regard to the risk of rebleeding, predictive scoring systems have been validated and can be used for the stratification of individuals as low, intermediate or high risk. These practical models may be used to guide the decisions on the therapeutic approach and follow-up, aiming to improve the clinical outcomes of patients with MGB.

Saurin classification/score

In 2003, a simple classification for the clinical relevance of lesions detected in CE was proposed [19]. It has since become a widely known as Saurin score. With this classification, lesions detected on SB CE are graded as P0, P1, and P2, according to the potential of clinically significant bleeding (► **Table 3**). Saurin score has been validated by i) identical grading of highly relevant (P2) lesions by CE readers in a blind tandem study in 100% of cases, as compared to 73% and 27%, respectively for P1 and P0 lesions; ii) high therapeutic impact 61% for P2 lesions versus 23% for P1 or P0 lesions; and iii) patient clinical follow-up [20]. More recently, a P3 category was included to indicate actively bleeding lesions [21]. The recent ESGE position on CE recommends Saurin score as a useful tool in the setting of OGIB [22], but can be easily adapted, in other clinical scenarios such as CE for example in Lynch syndrome, where the relevance of images is of high importance in the decision-making [23]. We advise its use in routine practice to force CE readers to think about decision-making at the time of CE reading [24].

Yano-Yamamoto classification/score

The Yano-Yamamoto classification was originally devised for device-assisted enteroscopy (DAE), as real-time evaluation of lesion’s pulsatility was a requisite for accurate classification,

► **Table 1** International Delphi Consensus on the nomenclature and descriptions of the most frequent SB vascular lesions.

Nomenclature	Semantic description	Nomenclature/description (%) agreement/strong agreement
Angiectasia/angiodyplasia	Clearly demarcated, bright-red, flat lesion, consisting of tortuous & clustered capillary dilatations, within the mucosal layer (surrounded by intestinal villi). Small (few mm) to large (few cm).	100%/93%
Erythematous patch	Small (few mm) & flat reddish area, without any vessel appearance, within the mucosal layer (surrounded by intestinal villi).	87%/80%
Red spot/dot	Miniscule (< 1 mm), punctuate, flat lesion with a bright-red area, without linear or vessel appearance, within the mucosal layer (surrounded by villi).	93%/80%
Phlebectasia	Small (few mm), flat-to-slightly elevated, bluish venous dilatation running below the mucosa (covered by villi).	93%/87%
Diminutive angiectasia ¹	Clearly demarcated, linear, bright-red lesion, consisting of tiny non-clustered capillary dilatations, within the mucosal layer (surrounded by villi).	73%/87%

SB, small bowel.
¹ consensus was not reached

► **Table 2** International Delphi Consensus on the nomenclature and descriptions of the most frequent SB inflammatory lesions.

Nomenclature	Description	Nomenclature/description (%) agreement/strong agreement
Aphthoid erosion	Diminutive loss of epithelial layering with a whitish center and a red halo, surrounded by normal mucosa.	85.2%/96.3%
Deep ulceration	Frankly deep loss of tissue compared to the surrounding swollen/edematous mucosa, with a whitish base	96.3%/85.2%
Superficial ulceration	Mildly depressed loss of tissue with a whitish bottom, whose features fit neither with that of aphthoid erosion nor with that of deep ulceration, as previously defined	81.5%/85.2%
Stenosis	Narrowing of the intestinal lumen withholding or delaying the passing of the videocapsule (therefore, to be evaluated on a video)	100.0%/88.9%
Oedema	Enlarged/swollen/engorged villi	85.2%/81.5%
Hyperemia	Area of reddish villi	96.3%/81.5%
Denudation	Reddish (but not whitish) mucosal area where villi are absent	81.5%/81.5%

SB, small bowel.

► **Table 3** Saurin classification (score) of bleeding potential of lesions in MGB.

Classification (type)	Examples	Risk of bleeding
P0	Phlebectasia, erythematous patch, diverticula without the presence of blood, nodules without mucosal break	No potential of bleeding
P1	Red spots, small or isolated erosions, possibly diminutive angiectasias	Low/uncertain
P2	Typical angiomas, large ulcerations, tumors, varices	High

being difficult to assess solely on the basis of lesion's morphology. However, this classification system of SB vascular lesions has been shown to contribute in stratifying SB lesions detected by either small bowel CE or DAE [25], based on their estimated bleeding risk. Literature data are scarce or conflicting regarding the magnitude of the risk and/or the potential benefit of endo-

scopic therapy for each type of lesion [26,27]. According to this classification system, angiectasias are considered Type 1 lesions, Dieulafoy's lesions are Type 2, and arteriovenous malformations are Type 3 (► **Table 4**, ► **Fig. 1**).

Comment: The Saurin classification has been validated and widely adopted. It is currently recommended as the method of

► **Table 4** Yano-Yamamoto classification.

Type	Description
1a	Red spot/angiectasia < 1 mm (with or without oozing)
1b	Angiectasia ≥ 2 mm (with or without oozing)
2a	Dieulafoy's lesion < 1 mm (punctulate lesion with pulsatile bleeding)
2b	Dieulafoy's lesion ≥ 2 mm (pulsatile red protrusion with pulsatile bleeding)
3	Arteriovenous malformation (pulsatile red protrusion with surrounding venous dilatation)
4	Atypical/unclassifiable

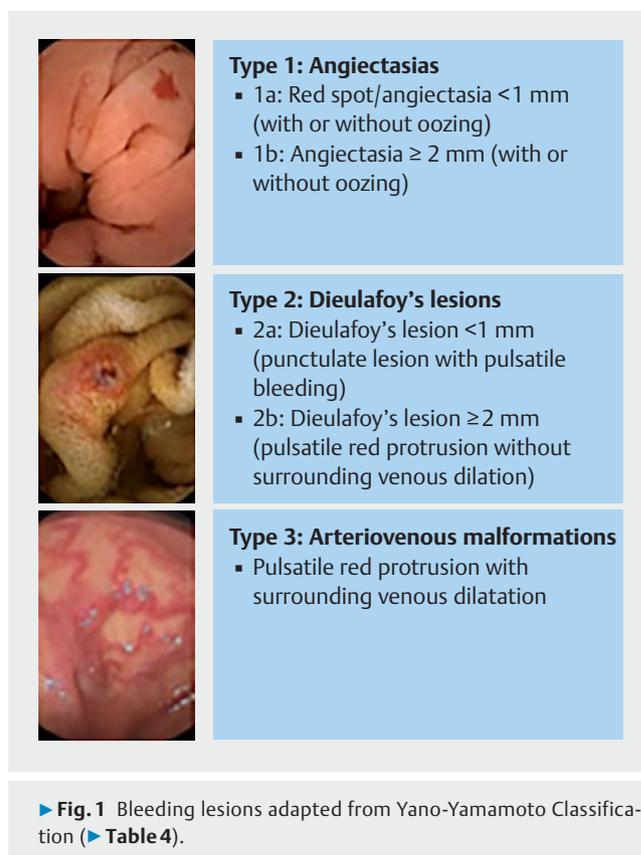
choice for evaluating the relevance of the lesions detected by SBCE in patients with MGB. Lesions classified as P2 are considered as having high potential of clinically significant bleeding.

Scores to predict the diagnosis of potentially bleeding SB lesions

Several clinical variables have been associated with a higher diagnostic yield (DY) of SBCE for potentially bleeding lesions. A study of almost 1,000 patients with OGIB showed that age > 60 years, overt bleeding and current hospitalization were all independent predictors for identifying a bleeding source on CE [28]. In patients with suspected SB bleeding, older age, overt bleeding, low hemoglobin (Hb) and increasing transfusion requirements have been consistently associated with the diagnosis of SB angiectasias [28–31]. Furthermore, a wide range of comorbidities were shown to associate with SB angiectasias, although results are inconsistent across studies, possibly due to significant heterogeneity in the design, population, length of follow-up, lack of standardized management or follow-up modality, and/or interobserver variability of CE interpretation.

A positive association has been described in patients with cardiovascular disease, mainly aortic stenosis (Heyde's disease) [32], heart failure with implantation of left ventricular assist device [33], ischemic heart disease [34], venous thromboembolism [35], von Willebrand's disease [36], chronic kidney disease (mainly late stages or dialyzed patients) or liver cirrhosis (mainly associated with portal hypertension) [37], among others. The use of anticoagulants and/or antiplatelet drugs has also been associated with an increased DY of SB CE, although it remains unclear whether these drugs are directly responsible for lesions' occurrence, or only contribute to the induction of bleeding from preexisting lesions, leading to the investigation and diagnosis of potentially bleeding lesions that could have remained clinically silent and undetected otherwise [38–40].

With the purpose of increasing the accuracy to predict the diagnosis of significant SB lesions in patients with suspected MGB, two scoring systems have been recently devised and are readily available for use in clinical practice: the Suspected Small Bowel Bleeding (SSB) Capsule Dx score [41] and the Ohmiya score [42]. These practical scores are expected to contribute



to guide the diagnostic workflow while improving patients' selection for SBCE.

Suspected Small Bowel Bleeding Capsule Dx score

A large multicenter cohort study of patients with suspected SB bleeding identified age > 54 years, Hb < 6.4 g/dL and inpatient status with overt bleeding as independent predictors for identifying a clinically significant diagnosis on CE [41]. Subsequently, a sensitive scoring system was successfully validated, being able to contribute for the decision of limiting the use of SB CE in low-risk patients (► **Table 5**, ► **Fig. 2**).

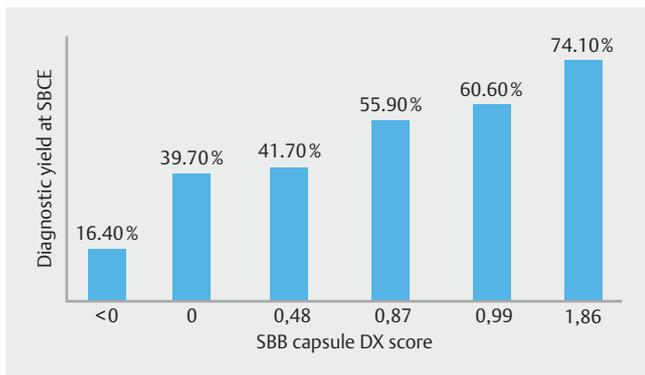
Ohmiya score

Ohmiya et al. developed a weighted comorbidity index based on various comorbidities which were associated with the development of SB vascular diseases and recurrent bleeding (► **Table 6**, ► **Fig. 3**) [42]. The final score results of the sum of the points attributed to each of the comorbidities of the patient, varying from 0 to 22 points. The ratio of SB vascular disease to nonvascular disease increases along with the Ohmiya score (< 30% if index < 2, and higher than 50% if index ≥ 2). Interestingly, when combining the age of the patient (younger or older than 50 years) and the Ohmiya index, the authors were able to further stratify the different SB haemorrhagic diseases. Indeed, onset age ≥ 50 years and index score < 2 identified patients with inflammatory disease, drug-induced injuries, or tumors with 72% accuracy, while an index score ≥ 2 identified patients with SB vascular diseases with 68% accuracy, regardless of age. Furthermore, the Ohmiya score also proved to be useful

► **Table 5** SSB Capsule Dx score.

SSB Capsule Dx score		Yes	No
A	Patient admitted to hospital with overt bleeding	1	0
B	pre-VCE hemoglobin of less than 6.4 g/dL	1	0
C	Age > 54 years old	1	0

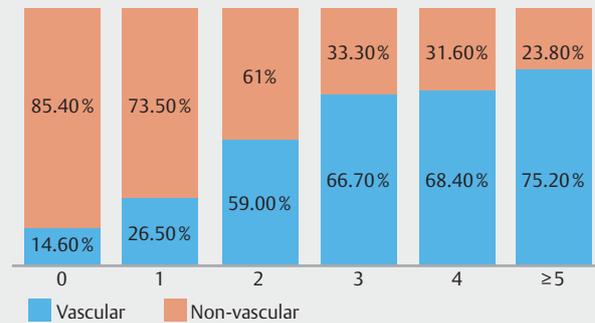
SSB Capsule Dx score = (0.87 x A) + (0.99 x B) - (1.38 x C)
SSB, small bowel bleeding; VCE, video capsule endoscopy.

► **Fig. 2** Diagnostic yield at SBCE per SSB Capsule Dx score.► **Table 6** Ohmiya Score.

Condition	Scoring points
Angina pectoris	1
Arrhythmia	1
Congestive heart failure	2
Chronic kidney disease	3
Hemodialysis	3
Peripheral vascular disease	3
Valvular heart disease	3
Portal hypertensive disease	3
Hereditary vascular disease	3

for the prediction of rebleeding: 33% of patients with scores ≥ 2 had recurrence of bleeding, versus only 15% of patients with scores < 2 (hazard ratio for score ≥ 2 , 1.729; 95%CI, 1.038 to 2.882; $P = .0355$).

Comment: A few scoring systems are currently available for predicting the diagnosis of SB lesions in patients with OGIB, such as the SSB Capsule Dx score and the Ohmiya score. Those scores have the potential to optimize the diagnostic algorithm and clinical management of patients with suspected SB bleeding, by prioritizing access to CE.

► **Fig. 3** SB vascular lesions ratios (vs. non-vascular diseases) for Ohmiya comorbidity index.

Clinical factors associated with SB angiectasias in patients with obscure GI bleeding

- Age > 60 years
- Use of anticoagulants
- Overt bleeding
- Severe anaemia ($\leq 7\text{g/dL}$)
- Increasing transfusion requirements

► **Fig. 4** Clinical factors associated with SB angiectasias.

Scores for assessing the risk of rebleeding in patients with known SB lesions

Patients with SB angiectasias have a significant risk of rebleeding, mainly during the first 2 years after the initial event [43, 44]. Data converge to the conclusion that advanced age [45, 46] and medication with anticoagulants [47, 48] are among the significant independent factors increasing the risk of rebleeding (► **Fig. 4**). There is ongoing debate on the efficacy of endoscopic treatment of SB angiectasias in reducing the risk of rebleeding [49, 50]. A recent meta-analysis found a rebleeding rate of 45% in patients with SB angiectasias after endoscopic treatment [51], although an overall decrease in transfusion requirements has been described even for some of the patients who experience recurrence of bleeding [52–54].

Many other clinical variables have been associated with an increased risk of rebleeding, such as overt bleeding [55], low hemoglobin level with higher transfusion requirements [56, 57], CE positive findings [58, 59], ≥ 3 angiectasias [60, 61], lesion size [62], proximal location in the SB [63, 64], Yano-Yamamoto classification [25], chronic renal disease [65, 66], cirrhosis [43], cardiac disease [21, 60], antiplatelet or nonsteroidal anti-inflammatory drug (NSAID) use [47], among others. Besides the aforementioned Ohmiya score, other scoring systems with clinical applicability have been recently devised for this purpose, integrating and weighting many of the described poten-

► **Table 7** RHEMITT score: variables and scoring points.

	Hazard ratio (CI 95%)	P value	Score points
Renal disease ¹	3.1 (2.0–5.0)	<0.001	3
Heart failure	1.6 (1.0–2.6)	0.044	1
Endoscopic findings ²			
P1 lesions	2.2 (1.1–4.2)	0.021	2
P2 lesions	2.5 (1.4–4.6)	0.002	3
Major bleeding ³	5.9 (2.7–13.1)	<0.001	5
Incomplete SBCE	2.0 (1.1–3.8)	0.031	2
Tobacco consumption ⁴	1.9 (1.2–3.1)	0.006	2
Treatment (endoscopic)	2.3 (1.4–3.8)	0.002	2

¹ Stage 4 or 5 chronic kidney disease.

² Saurin classification (only the higher rating accountable).

³ Bleeding causing a fall in hemoglobin level of ≥ 2 g/dL or leading to transfusion of ≥ 2 units of red blood cells.

⁴ ≥ 10 cigarettes/day.

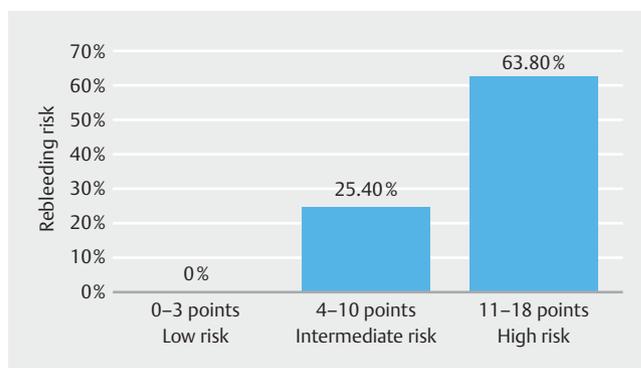
tial predictive factors to give a magnitude of the risk of rebleeding for each individual patient, allowing physicians to objectively stratify the risk and tailor the follow-up strategy accordingly.

RHEMITT Score

The RHEMITT score [67] demonstrated good accuracy for stratifying the risk of rebleeding in patients with MGB (area under the curve ROC 0.842, 95%CI 0.757 to 0.927). Three rebleeding risk groups were established: low (0–3 points); intermediate (4–10 points); and high (+11 points) (► **Table 7**, ► **Fig. 5**). Recently, an external validation cohort confirmed the usefulness and accuracy of the RHEMITT score in predicting rebleeding after SBCE [67]. Besides occurring more frequently, rebleeding also tends to occur earlier in intermediate (4–10 points) and high-risk patients (≥ 11 points) [67,68]. The RHEMITT score may contribute to assist physicians in the follow-up of patients with MGB, ultimately aiming to decrease the risk of rebleeding events, by means of optimized surveillance intervals and rational allocation of resources.

Predicting Rebleeding in Small Bowel Bleeding (PRSBB) Score

Uchida et al. developed and validated a nomogram which is able to predict the risk of rebleeding and to guide a risk-stratified follow-up strategy in SB bleeding patients [69]. It is based on eight independent risk factors for rebleeding: age, sex, SBB type, transfusion requirement, cardiovascular disease, liver cirrhosis, CE findings, and treatment (► **Fig. 6**). Cumulative rate of rebleeding was 3.6% for low-risk, 12.8% for intermediate-risk and 23.4% for high-risk patients (► **Fig. 7**). As most rebleeding events occurred within 2 years in low-risk patients and within 3 years in intermediate- or high-risk patients, the authors suggest that follow-up should be planned accordingly.



► **Fig. 5** RHEMITT score: rate of rebleeding per stratification of risk.

Furthermore, the same authors developed and validated a simple scoring system to determine the necessity of double-balloon enteroscopy (DBE) in OGIB [70], according to the stratification of rebleeding risk based on the three independent predictors, identified by multivariate logistic regression: OGIB type, blood transfusion, and CE findings. This scoring system yielded a maximum summative score of 7 points (► **Table 8**). The prediction score showed accuracy with an area under the receiver operating characteristics curve of 0.77. The sensitivity, specificity, positive predictive value, and negative predictive value at a cut-off ≥ 2.5 points were 72.5%, 74.6%, 72.6%, and 74.5%, respectively.

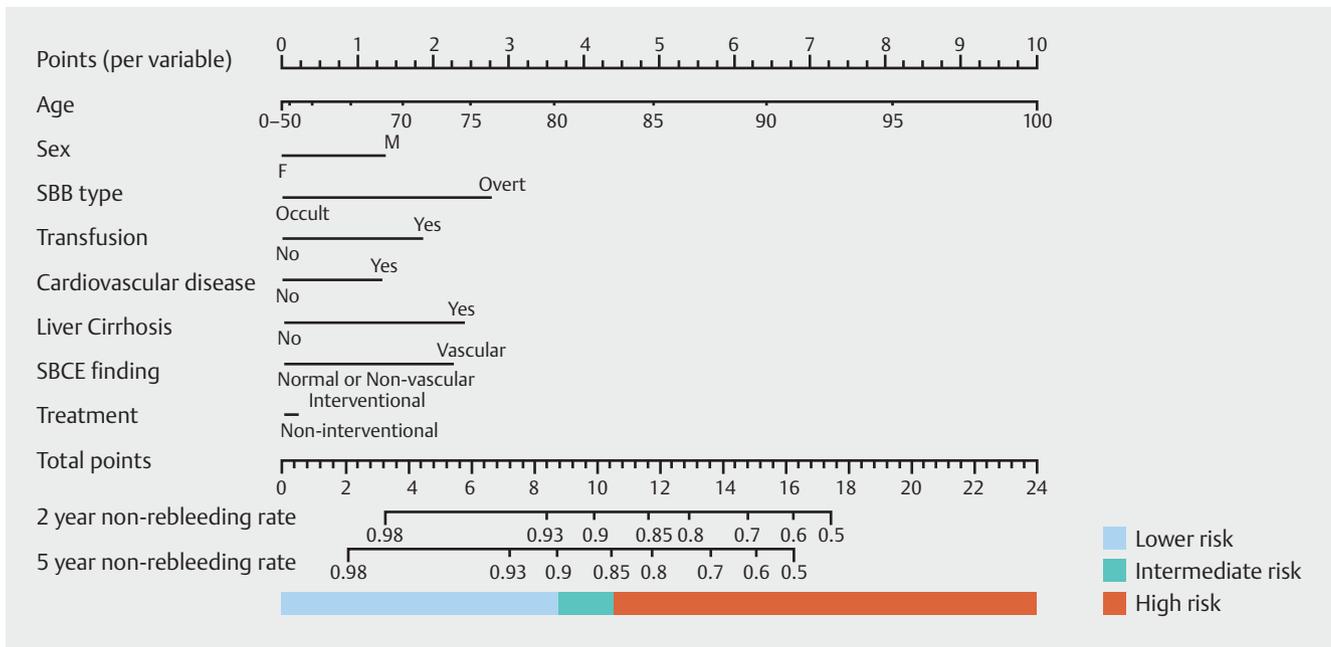
Niikura et al. predictive model of rebleeding in OGIB

In a large multicenter cohort study, Niikura et al. identified five potential risk factors (female gender, cirrhosis, warfarin use, overt bleeding, positive CE) for rebleeding during the follow-up of patients with OGIB (► **Table 9**, ► **Fig. 8**) [71]. The cumulative incidence of rebleeding was 11.0% at 12 months and 35.3% at 60 months. The rebleeding rate was 0% in patients with no predictors and 40% in patients with four or more predictors ($P < 0.01$). Moreover, patients with all the predictors required more transfusions, longer length of stay, and mortality was higher ($P < 0.01$).

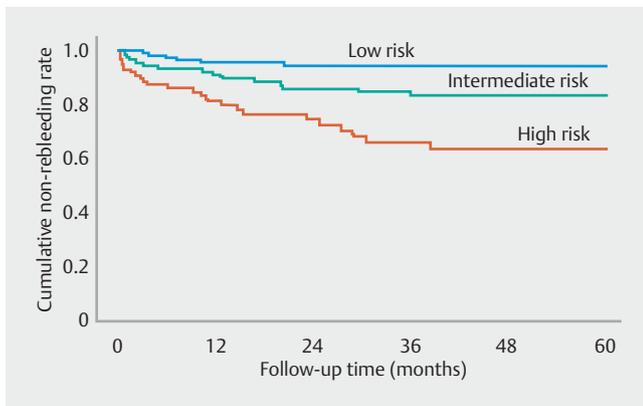
The authors considered these findings useful for decision-making when assessing and treating patients with OGIB in daily clinical practice, recommending as follow-up: (1) no follow-up for patients with no risk factors; (2) follow-up for 1 year at 3- to 6-month intervals in patients with any of the risk factors (approximately 20% rebleeding rate at 1 year); (3) follow-up for > 1 year at 3- to 6-month intervals in patients with four or more risk factors (40% rebleeding rate during a 1.5-year period).

ORBIT Score

The ORBIT score was originally created to predict major bleeding in patients with atrial fibrillation and chronic anticoagulation [72]. It represents an acronym composed of five clinical variables, ranging from 0 to a maximum of 7 points, and it has been recently adapted to patients presenting with MGB submitted to CE (► **Table 10**, ► **Fig. 9**) [73]. The mean interval of the follow-up was 35 months (range: 6 to 103 months). In high-risk patients, rebleeding was significantly more common than



► Fig. 6 PRSB score nomogram.



► Fig. 7 Cumulative non-bleeding rate.

in low/intermediate-risk patients (80.0% vs. 36.6%; $P=0.003$). The authors concluded that due to the increased risk or rebleeding, patients with an ORBIT score of 4 points or more should have a closer follow-up and proactive diagnostic and therapeutic management.

Comment: Scoring systems such as the PRSB and, most recently, the RHEMITT score have been validated and can be used for the stratification of individuals with documented MGB as low, intermediate, or high risk of rebleeding. These scores are readily available for clinical practice while planning the follow-up and therapeutic approach, aiming to improve the clinical outcomes of patients with MGB.

► Table 8 Double-balloon endoscopy score.

	0	1	2	4
OGIB type	Occult	Previous	Ongoing	–
Blood transfusion	No	Yes	–	–
SBCE findings	Normal/erosion	Ulcer	Vascular lesion	Tumor

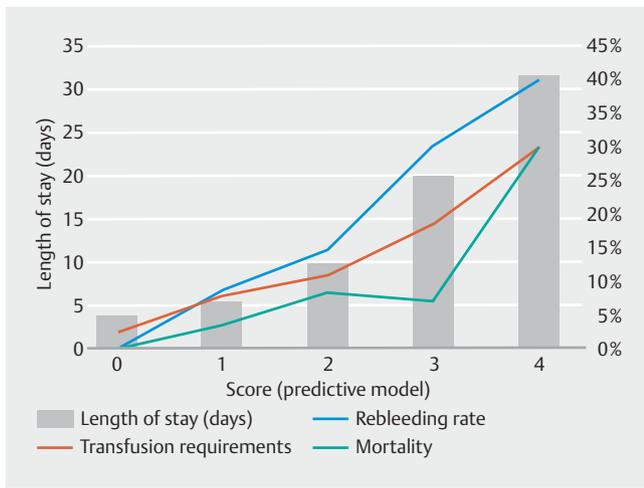
Scores 0–2 (52.3% of patients): low necessity of DBE
 Scores ≥3 (47.7% of patients): high necessity of DBE
 OGIB, obscure gastrointestinal bleeding; SBCE, small-bowel capsule endoscopy; DBE, double-balloon endoscopy.

► Table 9 Niikura et al. predictive model: risk factors associated with clinical outcomes.

Risk factors (n)
Female gender
Cirrhosis
Warfarin use
Overt bleeding
Positive SBCE
SBCE, small-bowel capsule endoscopy

Lesion localization indices

When a lesion is detected by CE, choosing the optimal insertion route for DAE is a pivotal step in patient management. The correct choice helps to minimize the number of endoscopic examinations with no or limited yield and provides a cost-effective &



► **Fig. 8** Niikura et al. predictive model: association with clinical outcomes.

precision approach [15, 74–76]. The location of a lesion in the SB can be estimated by CE time-based indices, expressed as the time taken for the capsule to reach the lesion divided by the examination's total transit time (TT). Some software modes show the percentage of SB TT for each image (► **Fig. 10**). Additional AI-tools as progression indicator aim to modify the time-based calculation into a SB length-estimation by including measurement of capsule movement. This can lead to quite divergent TT intervals corresponding to length-based tertile-calculation. If a graphic localization image is also available, areas of evident delay in transit can be counter-checked and taken into account for planning enteroscopy access.

Eventually, the choice of the route of insertion is based on a specific cut-off, decided a priori by the team: if the lesion is detected within this cut-off the approach will be antegrade, and conversely. But which is the most reliable cut-off? Several studies have been conducted on this premise, mainly differing in the DAE technique used and the CE landmarks that are taken into consideration.

The concept of CE TT in DAE insertion route selection was first analyzed by Gay et al. [76], using an index based on the time from capsule ingestion to caecum, with a ratio cut-off of 0.75. When the lesion was located at $\geq 75\%$ of the total TT, the positive predictive value (PPV) and negative predictive value (NPV) for a retrograde approach were 94.7% and 96.7%, respectively. The main limitation of this index is the inherent variability of the gastric TT. To overcome this, subsequent studies took into account the TT from the pylorus (or the first duodenal image) to the caecum (or ileocecal valve). A cut-off of 0.5 was proposed by Nakamura et al. [77] and Maeda et al. [78], whereas Li et al. [79] and Lin et al. [80] proposed a cut-off of 0.6 and 0.66, respectively. According to Chalazan et al. [81] the best-performing cut-offs for antegrade and retrograde DAE were 0.57 and 0.74, respectively. Furthermore, Tsuboi et al. [82] validated the role of the integrated PillCam Progress indicator a progression-based index, used with a cut-off of 0.5. It

► **Table 10** ORBIT score: risk of rebleeding in patients with suspected mid-gastrointestinal bleeding under chronic anticoagulation.

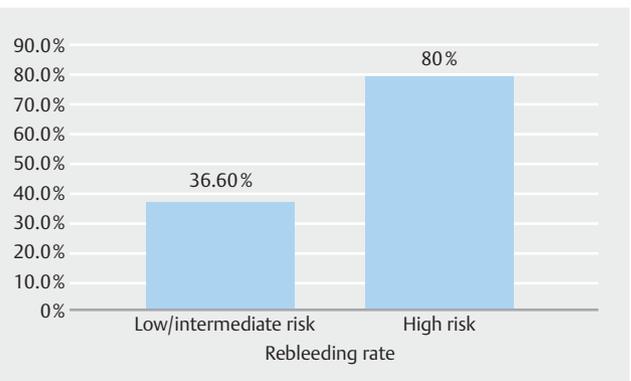
	Points assigned
Older age (≥ 75 years)	1
Reduced hemoglobin ¹	2
Bleeding history ²	2
Insufficient renal function ³	1
Treatment with antiplatelets ⁴	1

¹ Hemoglobin < 12 g/dL for women or < 13 g/dL for men or hematocrit $< 36\%$ for women or $< 40\%$ for men.

² Any history of gastrointestinal bleeding or intracranial bleeding, i. e., epidural hematoma, subdural hematoma, subarachnoid haemorrhage, or intracerebral or intraventricular hemorrhage.

³ Estimated glomerular filtration rate < 60 mg/dL/1.73 m².

⁴ Aspirin, ticagrelor, prasugrel, clopidogrel or fixed-dose combination aspirin-dipyridamole.



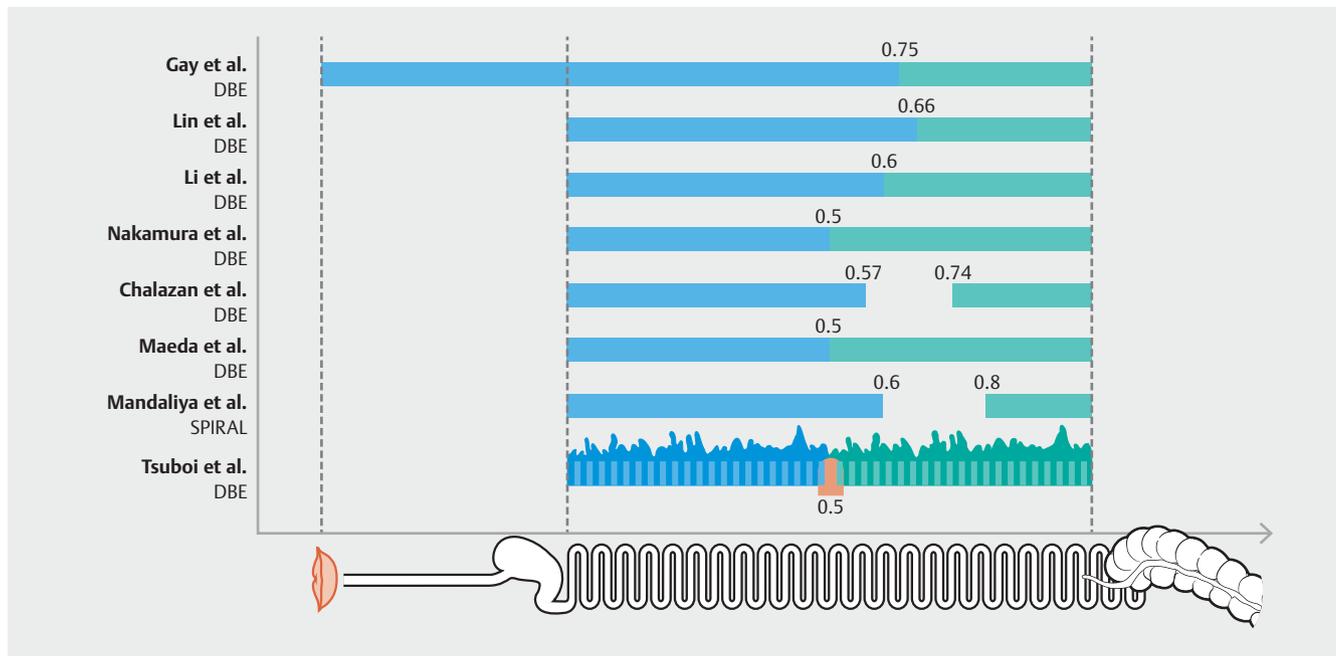
► **Fig. 9** ORBIT score: rate of rebleeding per risk stratification.



► **Fig. 10** 3D localization trace with SB in green. Bar on the right presents the SB length travelled. 2D localization trace showing capsule passing the duodenum and reaching the proximal jejunum. On the right, similarity of images (corresponding to low speed) is increasing (higher amplitudes) towards the distal SB. Percentage of transit is displayed.

is worth noting that DBE was the chosen DAE technique in all of these studies.

Although the proposed cut-offs differ slightly, in terms of SB percentage, they all had acceptable performances with the following success rates: Li et al., 100%; Lin et al., 100%; Maeda et al., 78.3%; Tsuboi et al., 96%. PPV and sensitivity were 97% and 90% in the study by Nakamura et al., whereas Chalazan et al. reported 75% and 75% for antegrade approach and 78% and 88% for retrograde approach. Recently, Mandaliya et al. [83] con-



► **Fig. 11** A graphical representation of the transit time- and progression-based localization scores.

firmed the usefulness of a capsule lesion index with spiral enteroscopy (SE), using the first duodenal image and the first cecal image as landmarks. Antegrade and retrograde SE were performed with index <0.6 and >0.8 , respectively: for lesions in between 0.6 and 0.8 an individualized approach was suggested. A clear schematic overview of the indices is shown in ► **Fig. 11**.

Comment: Although tested indices may differ in cut-offs and landmarks, their overall outcomes are highly successful. An SB TT $<50\%$ clearly favors antegrade approach for DBE, and $>75\%$ a retrograde approach, respectively. Divergent results between these thresholds reflect the difficulty of reaching the mid-SB and warrant an individual approach. To note, in doubtful cases (e.g., the lesion is located spot at the cut-off value) the antegrade approach is the one to be preferred, for both technical and clinical reasons.

Inflammatory scores in CE

CD can affect the entire gastrointestinal tract. The extent and severity of SB inflammation can be assessed with computed tomography enterography, magnetic resonance enterography, intestinal ultrasound (US) and/or CE. CE is considered the most sensitive of these modalities with a particular advantage in evaluating proximal SB mucosal involvement [84]. Other causes of SB inflammation include NSAIDs-induced enteropathy, coeliac disease with ulcerative jejuno-ileitis, lymphoma, radiation enteritis, opportunistic infections, intestinal tuberculosis, HIV, and Bechet's disease [85].

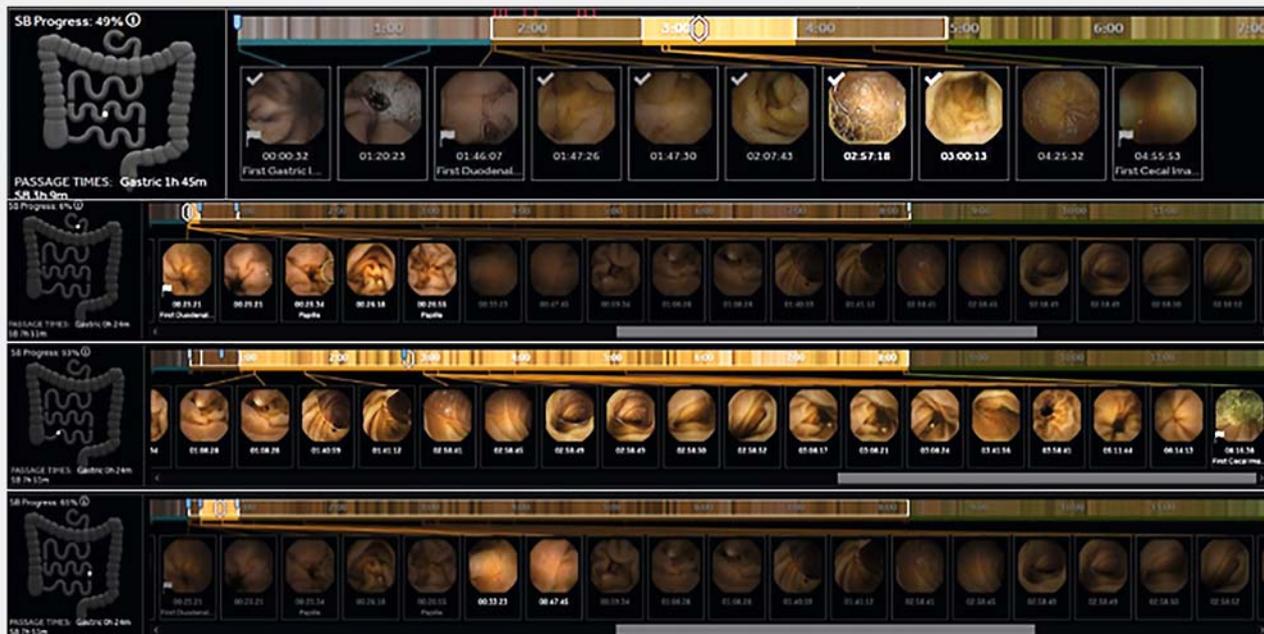
There are different ways to measure the response of inflammation to different treatments. Endoscopic measures of inflammation, for example, the CD Endoscopic Index of Severity or the simple endoscopic index of severity, take into account

parameters like deep or superficial ulcerations and their surface, but these scores can only assess areas that are within the reach of the colonoscope, i.e. colon and terminal ileum. The invention of CE introduced the need for quantitative metrics to assess mucosal inflammation. Furthermore, as treatment targets focus on the importance of mucosal healing, this has become even more essential. Several quantitative inflammatory scores for CE have been developed over the years, some for SB only and some for both SB and the colon.

Inflammatory scores SB CE

Lewis score

The so-called Lewis score (LS) was the first inflammatory score that was introduced and is the most widely used index, as it is embedded in the CE RAPID software (Medtronic, United States). In this, SB is artificially divided into three parts according to the TT (from the first duodenal image to the first caecal image), so that three tertiles are obtained. The division, however, is on an artificial basis; these tertiles are actually determined by time and not by SB length, thus allowing proximal tertiles more pronouncement if the capsule stays for a long time in the ileum/terminal ileum. New software algorithms aim to modify the tertiles by including capsule movement calculation (► **Fig. 12**). For each of the tertiles, there is a scoring index that includes three endoscopic variables: villous edema, ulcerations and stenosis. Index parameters are measured by number (none, single, few 2–7, multiple i.e. ≥ 8), longitudinal extent (short segment $<10\%$, long segment 10–50%, whole tertile $>50\%$) and additional descriptors (circumferential extent, etc.) (► **Table 11** and ► **Fig. 13**).



► **Fig. 12** SB divided into three tertiles (top image). AI-assisted division of SB into three tertiles of estimated equal length, corresponding to very different transit times each: proximal SB (upper row), mid SB (lower row), and distal SB (middle row). On the left of each row, a white point presents the localization of the capsule in a pictogram solely as estimated by modified transit time.

The score is calculated separately for each tertile and the final score is the highest of the three. A score < 135 is designated normal or clinically insignificant mucosal inflammatory change; a score of $\geq 135 - < 790$ = mild inflammation; and, ≥ 790 = moderate-to-severe inflammation [86]. The score was validated by showing a strong inter-observer agreement for the determination of the LS in a monitoring established CD [87]. LS was found to be effective both in diagnosing CD and assessing the extent of the disease and in monitoring and evaluating response to treatment. In a retrospective study, CD was ultimately diagnosed in 82.6% of patients with significant inflammatory activity on CE (LS > 135), but in just 12.1% of those having a LS < 135 ($P < 0.05$). The PPV, NPV, sensitivity and specificity were 82.6%, 87.9%, 82.6%, and 87.9%, respectively [88]. Another study included patients who underwent CE for suspected CD according to the criteria of the International Conference on Capsule Endoscopy (ICCE) [89]. LS (cut-off > 135) showed a good diagnostic accuracy of CD, with an area under the curve of the receiver operating characteristic (AUROC) of 0.93 ($P < 0.001$). There was a significant association between a higher LS and the need for immunomodulatory therapy, biological therapy, bowel resection surgery or hospital admission due to a CD flare-up within the first year after diagnosis.

In a recent study on CD patients in remission, different measures were examined, in their ability to predict flare-ups. Quantitative assessment of SB inflammation on CE was the most accurate predictor of relapse within 2 years, i. e. a baseline LS > 350 points predicted imminent disease exacerbation within 6 months to 2 years [90].

Capsule Endoscopy Crohn's Disease Activity Index (CECDAI)/Niv score

The score divides the SB into proximal and distal segments according to the midpoint of SB TT. Each segment is rated on the basis of three parameters, each rated on a scale of 0 to 3 or 5 points: A – inflammation (erythema, hyperaemia and edema, denudation, nodularity, aphthae, erosion, ulcer and bleeding); B – extent of disease (focal, patchy and diffuse); C – presence of narrowing (single-passed, multiple passed and obstruction). The segmental score is calculated by multiplying the inflammation sub score by the disease extent sub score and adding the stricture sub score ($A \times B + C$); the final score is calculated by adding the two segmental scores: total CECDAI = $(A1 \times B1 + C1) + (A2 \times B2 + C2)$ [91] (► **Table 12**). In 2012, the score has been validated later on by in a multicenter study led by the same group [92].

Several studies compare CECDAI to the LS. Two retrospective studies found significant correlation between LS and CECDAI (rs values of 0.6324 and 0.878, $P < 0.0001$) [93, 94]. In a prospective study of patients with established CD in clinical remission, moderate correlation between the worst segment LS and CECDAI was demonstrated (Pearson's $r = 0.66$, $P = 0.001$), while a stronger correlation was found between the cumulative LS and CECDAI ($r = 0.81$, $P = 0.0001$) [95]. Interestingly, these studies defined very different threshold levels of CECDAI; in the retrospective studies mentioned above, CECDAI level of 3.8 and 7.7 corresponded to LS threshold of 135 [93, 95] and CECDAI level of 5.8 and 10.3 corresponded to LS threshold of 790 [93, 95]. In the latter prospective study, CECDAI level < 5.4 corresponded to

► **Table 11** Lewis score parameters and descriptors.

Rated for each tertile						
Parameters	Number		Longitudinal extent		Descriptors	
Villous appearance	Normal	0	Short segment	8	Single	1
	Edematous	1	Long segment	12	Patchy	14
				Whole tertile	20	Diffuse
Ulcer	None	0	Short segment	5	<1/4	9
	Single	3	Long segment	10	1/4–1/2	12
	Few	5	Whole tertile	15	>1/2	18
	Multiple	10				
Stenosis – rated for whole tertile						
	None	0	Ulcerated	24	Traversed	7
	Single	14	Non-ulcerated	2	Not traversed	10
	Multiple	20				

Lewis score: Score of the worst-affected tertile [(villous parameter × extent × descriptor) + (ulcer number × extent × size)] + stenosis score (number × ulcerated × traversed).

► **Fig. 13** Lewis score (LS) calculator, integrated in the PillCam RAPID reader.

LS <135, while CECDAI >9.2 corresponded to LS >790 [94]. Thus, while the threshold values of the LS are constant, the threshold values of the CECDAI score are different among different studies, making it difficult to interpret and to clinically correlate [93–95].

Correlation between CE findings and clinical indices or laboratory biomarkers is moderate, and this is reflected in the

correlation to the inflammatory scores. For example, in a retrospective study, neither C-reactive protein (CRP), nor the Harvey Bradshaw Index correlated with LS ($r_s=0.068$, $P=0.72$; $r_s=-0.15$, $P=0.40$) or CECDAI ($r_s=0.004$, $P=0.98$; $r_s=0.10$, $P=0.23$) [95]. Another study demonstrated a moderate correlation between LS and fecal calprotectin (FC) ($r=0.44$) becoming more evident in patients with FC of 100 mg/g ($r=0.67$). No cor-

► **Table 12** Capsule endoscopy Crohn's disease activity index (CECDAI) scoring system.

A. Inflammation score	
▪ None	0
▪ Mild to moderate edema/hyperemia/denudation	1
▪ Severe edema/hyperemia/denudation	2
▪ Bleeding, exudate, aphthae, erosion, small ulcer (>0.5 cm)	3
▪ Moderate ulcer (0.5–2 cm), pseudopolyps	4
▪ Large ulcer (>2 cm)	5
B. Extent of disease score	
▪ None	0
▪ Focal disease (single segment)	1
▪ Patchy disease (multiple segments)	2
▪ Diffuse disease	3
C. Narrowing (stricture)	
▪ None	0
▪ Single-passed	1
▪ Multiple-passed	2
▪ Obstruction	3
Segmental score: AxB + C	
Total score: (A1xB1 + C1) + (A2xB2 + C2)	

relation with FC was demonstrated for CECDAI [93]. In a prospective study, there was a moderate correlation between CE scores and FC levels ($r=0.39$, $P=0.002$ for LS, $r=0.48$, $P=0.001$ for Cumulative LS, and $r=0.53$, $P=0.001$ for CECDAI, respectively). CRP levels were not significantly correlated with either score [94]. In the largest retrospective study to date, a poor correlation between LS and FC was reported ($r=0.16$) [96].

There were other attempts to create scoring indices specifically for use with CE: Buchman et al graded CE videos as grade 0 (normal); grade 1 (erythema, isolated villi loss); grade 2 (erosion, no ulcer); or grade 3 (ulcers, spontaneous bleeding and/or stricture). The study was undertaken to determine the accuracy of CE in the diagnosis of CD relative to small bowel follow-through (SBFT) and clinical/laboratory indices of CD activity. It was done by evaluation of the occurrence of active disease in patients with known CD. CE and SBFT scores highly correlated ($r=0.65$, $P=0.001$). Neither CE nor SBFT scores correlated with biological or clinical indices [97]. Graham et al. assessed SB mucosal inflammation in patients taking NSAIDs. Lesions were described as red spots, small erosions, large erosions or ulcers. They defined mild injury as few or no erosions, and absence of large erosions/ulcers. Major injury was defined as >4 erosions or large erosions/ulcers and provided endoscopic evidence that SB mucosal injury is very common among chronic NSAIDs users (► **Table 13**) [98].

► **Table 13** Pros and cons of Lewis score and CECDAI.

	Pros	Cons
Lewis score	Validated	Segments not accurate (by time)
	Embedded in software	Score strongly influenced by stricture
	Easy to use	
CECDAI	Validated	Segments not accurate (by time)
	Comparable to Lewis score	Not embedded in software
	Can be used for colon as well	Score strongly influenced by stricture

SB & colon inflammatory scores

Capsule Endoscopy Crohn's Disease Activity Index (CECDALic/Niv score) for SB and colon

An extension of CECDAI or Niv score was published in 2018. It is based on the same parameters and the same calculations as in the SB with the addition of two colonic segments, proximal and distal, a total of four segments. The range of CECDALic score is between 0 and 72 [99]. This score was examined and validated demonstrating excellent agreement between three observers. In addition, a very good correlation between CECDALic and calprotectin ($r_s=0.82$; $P=.012$) and a moderate correlation with C-reactive protein ($r_s=0.50$; $P=.019$) was shown [100].

Panenteric Crohn's Capsule Score (PCCS)/Eliakim Score (ES)

Recently, a novel pan-enteric capsule, PillCam Crohn's (Medtronic, United States), was approved for use. It allows a comprehensive view of the whole intestine [101]. In this score the whole bowel is divided by length into five segments; the small intestine is divided into three tertiles and the colon is divided into two: right colon and left colon. The score takes use of the new Crohn's specific software (Rapid 9) of the new capsule. The score is calculated separately for each segment using the following parameters: A – the most common lesion (graded by severity as 1–3), B – the most severe lesion (graded by severity as 1–3), C – approximated disease extent (0%, 0% to 10%, 10% to 30%, 30% to 60%, 60% to 100%), and D – stricture. The score is calculated separately for each one of the five segments: Segmental score ((A + B) × C) + D (► **Table 14**). The final score is calculated by adding the five segmental scores. The score for the three segments of the small intestine was calculated separately by adding them to create the Small bowel PCC (PCCS-SB) score. It was compared to LS and a strong correlation ($r=0.8$ for reader 1 and $r=0.82$ for reader 2, $P<0.001$ for both) was found between the scores. The calculation of the cut-off values is LS 135 = 4, LS 350 = 5, LS 790 = 8 [102].

A final overview of the aforementioned scores is presented in ► **Table 15**.

► **Table 14** PillCam Crohn's disease capsule score.

A. Most common lesion (MCL)	
▪ None	0
▪ Mild	1
▪ Moderate	2
▪ Severe	3
B. Most severe lesion (MSL)	
▪ None	0
▪ Mild	1
▪ Moderate	2
▪ Severe	3
C. Extent of disease	
▪ None	0
▪ 0–10 %	1
▪ 10–30 %	2
▪ 30–60 %	3
▪ 60–100 %	4
D. Stricture	
▪ None	0
▪ One traversed	1
▪ > 1 traversed	2
▪ Retention	3
Segmental score: (A + B) × C + D	
SB PCC (PCCS-SB): SB1 + SB2 + SB3	
Panenteric PCC (PCCS): SB1 + SB2 + SB3 + RC + LC	
SB, small bowel; PCCS, panenteric Crohn's capsule; RC, right colon; LC, left colon.	

Aside CECDALic, all other descriptions or scores combining small & large bowel are not yet validated and currently should be used for research purposes only.

Scores to differentiate between SB mass or innocent mucosal bulge

Paradoxically, CE which is highly sensitive for millimetric mucosal breaks may overlook large masses, in particular in the proximal SB. A retrospective, single-center study showed a near 17% missing rate for tumors [103], in line with the first report of the low sensitivity of CE for masses [104]. An explanation of this paradox may be that a large mass, near the ligament of Treitz, exercise gravitational traction on the mobile bowel loop, hiding behind a fold, and stretching the proximal loop, so the capsule may assume a straight direction seeing it only tangentially (► **Fig. 14**).

There may be diagnostic confusion between a subepithelial mass and an innocent bulge (IB), bearing in mind that most of the sporadic benign and malignant tumors of the SB are subepithelial. IB is defined as a smooth, round protrusion of a normal-appearing mucosa, having an ill-defined boundary with the surrounding mucosa and a base larger than its height [105]. It is likely formed by the compression of an adjacent loop of the bowel tangle, and it is reported in up to 5% of consecutive CE [105, 106]. A subepithelial mass devoid of alarm features (i.e. ulcer, congestion, erosion, erythema, blood, clots) looks like an IB. To discriminate a subepithelial mass from an IB, SPICE (**S**mooth **P**rotruding lesion **I**ndex at **C**apsule **E**ndoscopy, ► **Table 16**) criteria have been developed and validated in a single-center, prospective study; a SPICE score >2 had sensitivity 83.3% (95%CI 36 to 99) and specificity 86.4% (95%CI 67 to 98) for subepithelial mass (AUROC 0.9; 95%CI 0.72 to 0.98) [105]. SPICE score was independently validated in two subsequent studies (► **Table 17**). Hatem et al, in a prospective series of 640 consecutive CE, found 30 patients with equivocal findings between IB and subepithelial mass. After diagnostic workup, three tumors were found; two of these (a car-

► **Table 15** Summary of inflammatory scores.

	SB	SB and colon	Colon
Lewis score	+ 86,87,88,90 ¹	–	–
Capsule Endoscopy Crohn's Disease Activity Index (CECDAI)/Niv score	+ 91,92 ¹	–	
Capsule Endoscopy Crohn's Disease Activity Index (CECDALic/Niv Score) for the small bowel and colon.	+ 91,92 ¹	+ 99,100 ¹	+
Panenteric Crohn's capsule score (PCCS)/Eliakim score	+	+ 100 ¹	+
Capsule Scoring of Ulcerative Colitis (CSUC)	–	–	+ 103 ¹

SB, small bowel.

¹ Reference number

cinoid and an ovarian metastasis) had a SPICE score >2 [106]. Rodrigues et al, in a retrospective series of 30 patients having a round, smooth protruding lesion, found 12 tumors; SPICE >2 showed a 66, 7% (95%CI 34,9 to 90) sensitivity, 100% (95%CI 81,5 to 100) specificity, (AUROC 100; 95%CI 81,5 to 100) [107].

More recently, Min et al – based on the fact that angle between the protrusion and the surrounding mucosa (corresponding to the first of SPICE criteria) is crucial in the differential diagnosis – calculated this angle with a protractor upon the computer screen on a retrospective series of SBCE. Twenty-five of 34 patients had a pathologic diagnosis of a tumor. In comparison with SPICE criteria, an angle lesser than 90 degrees had the same specificity but a higher sensitivity (92% vs 32%) in their series [108]. In this study, the final diagnostic assessment of patients diagnosed as IB, and the length of follow-up were unclear. However, there is little doubt that quantification with a protractor of the first SPICE criterion may be useful to reduce its subjectivity and interobserver variability. Further studies, using a protractor to better define the first SPICE criterion, using a cut-off <90° to assign 1 point to the final score, are warranted.

Another score, named herein Shyung score [109], was proposed by Shyung et al, in a retrospective study comprising 12 CE in patients (age range: 23 to 79 years) with suspected SB tumors. The features of the scoring system are summarized in ► **Table 18**. With a total score ≥4, the probability of SB mass lesions was high and in this small cohort, patients had ileal ectopic pancreas, melanoma, gastrointestinal lymphoma, and gastrointestinal stromal tumor. The probability of SB mass lesions in those with a score of ≤2 was low. Shyung score has not been validated in any other study.

Comment: The SPICE score has been validated as a reliable and practical tool for differentiating between innocent bulges (score ≤2) and subepithelial masses (score >2) in SBCE.

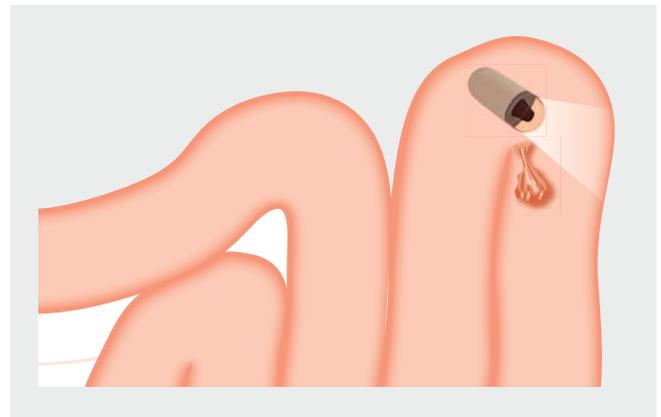
Cleanliness scores

SB CE cleanliness scores

As in traditional endoscopy, the quality of mucosal visualization and thus the DY of CE is dependent on the absence/presence of air bubbles, bile and intestinal debris. The evaluation of the quality of SB preparation is necessary to assess the accuracy of the findings in CE. During colonoscopy, the validated Boston Bowel Preparation Score provides an assessment of colon cleanliness [110]. Several scores assessing SB cleanliness have been proposed. These can be divided into operator-dependent or automated scores. The presence of a universal grading score would also contribute to standardize CE protocols and to compare the results of different methods of small-bowel preparation.

Automated scores

Apart from having an objective, reliable, and reproducible scoring system, performing this analysis in a timely manner is also important. Thus, computer generated scores could fulfill all these criteria (► **Table 19**) [111].



► **Fig. 14** Hypothetical mechanism by which a large mass may be missed on capsule endoscopy.

► **Table 16** SPICE score calculation¹

SPICE score	Score	
	No	Yes
Criterion		
Ill-defined boundary with the surrounding mucosa	1	0
Diameter larger than its height	1	0
Visible lumen in the frames in which it appears	0	1
Image of the lesion lasting > 10 minutes	0	1

SPICE, Smooth Protruding lesion Index at Capsule Endoscopy.
¹ A value >2 is predictive of subepithelial mass.

► **Table 17** Summary of studies.

		SB lesions	IB
Girelli et al	SPICE score	6	19
Rodrigues et al	SPICE score	12	18
Shyung et al	Shyung score	6	6
Min et al	Mucosal protrusion angle	25	9

SB, small bowel; IB, innocent bulge; SPICE, Smooth Protruding lesion Index at Capsule Endoscopy

Van Weyenberg et al developed a proof of concept, computed assessment of cleansing (CAC) score, based on objective measurements of color intensities of the red over green (R/G) channels of the tissue color bar of the Rapid Reader in the Pill-Cam CE system. This bar comprises the summary of all CE images. This was converted to the red-green-blue mode (RGB) and the relation between the mean intensity of the red and green channels was used as a measure of small-bowel cleanliness. The concept of R/G ratio is based on the fact that properly visible mucosa is associated with red colors whereas a fecal-contaminated lumen is associated with green. The mean intensity values of the green and red channels were determined using a histogram function of photo editing software [111]. This ap-

► **Table 18** Shyung score.

Criterion	Bleeding	MD	IS	Colour	WV	Total score
	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	
	1/0	1/0	1/0	1/0	1/0	>4

MD, mucosal disruption; IS, irregular surface; WV, white villi

► **Table 19** Small bowel cleanliness scales: Computer-dependent scales, quantitative scores.

Reference	Capsule system	Preparation	Assessment parameters	Proportion of video analyzed
Van Weyenberg et al	PillCam	2 L PEG	Mean intensity values of the green and red channels of the SB segment of the tissue colour bar	Tissue color bar – Entire video
Ponte et al	Microcam	Clear liquid diet, overnight fast	Mean intensity values of the green and red channels of the SB segment of the tissue colour bar	Map view bar – Entire video
Klein et al	PillCam	Clear liquid diet, overnight fast	Pixels of the SB segment of the tissue colour bar	Tissue color bar – entire video
Ali et al	PillCam	Clear liquid diet, split 1.5 L PEG, with or without metoclopramide	Red/green pixel ratio of still frame images	Tissue color bar of still frame images
Oumrani et al	PillCam	Not specified	Colorimetry (red/green ratio), abundance of bubbles, brightness	Still frame images

PEG, polyethylene glycol; SB, small bowel.

proach was then also used by Ali et al. Based on the R/G pixel ratio of still frame images, they assessed the quality of SB cleansing. A SB-CAC score cut-off of 1.6 demonstrated a sensitivity of 91.3% and a specificity of 94.7%, defining an adequate SB visualization [112].

This concept was also adapted to the OMOM and MiroCam CE systems. The MiroCam reading software, has a function named “Map View” and this is bar contains a representation of all the available recorded images recorded (► **Fig. 15a**, ► **Fig. 15b**). Using the same methodology as that for PillCam, through photo editing software, the mean intensities of the red and green channels were determined. The authors used two different types of photo editing software and had identical results, resulting in an intra-test reliability of 1.0 ($P < 0.001$) [113].

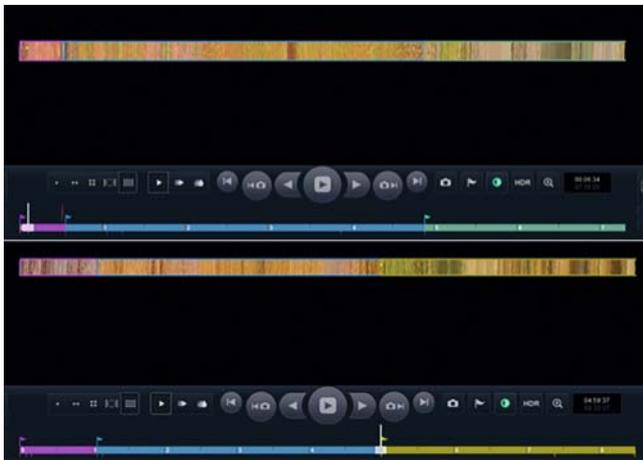
Similar to the above computed scores, Klein et al designed and validated a computer algorithm based on the pixels in the tissue color bar of the CE PillCam system. Each pixel of the bar was independently labeled as adequate or inadequate. These were defined based on the pixel color and hue derived from the pixel RGB values. The computer algorithm then calculated and summarized the total number of “inadequate” pixels, their locations, the “adequate” to “inadequate” pixel ratio and the longest duration of consecutive “inadequate” pixels in the color bar. The computed classification of bowel preparation when compared to the subjective opinion of the authors had a sensitivity of 95%, specificity 82% and a 90% accuracy [114]. A score allowing evaluation of the abundance of bubbles in CE still frames, based on Gray-level of co-occurrence matrix detector

strategy, was developed. Based on this a score making use of still frames was developed and categorized as presenting with < 10% or 10% of bubbles and suggest that a 10% cut-off as being adequate with a sensitivity and specificity of 95% (► **Fig. 16**) [115].

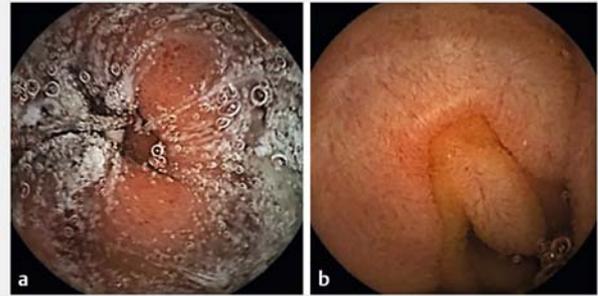
More recently, Oumrani et al proposed a score based on three electronic parameters – colorimetry, abundance of bubbles, and brightness are assessed. These parameters were compared to the Brotz score as assessed by different experts, with a score of 7/10 being adequate mucosal visualization. Through automated analysis, the combination of the R/G ratio, abundance of bubbles, and brightness achieved a sensitivity of 90.0% and a specificity of 87.7%, with optimal reproducibility. Limitations of this score analysis are that it has been performed on still frames and not video analysis and on normal videos of patients with OGIB [116]. Though numerous automated scores have been proposed, to date no practical readily available score is available on the CE reading software.

Operator-dependent scores

There are numerous studies that have evaluated the cleanliness of the SB through operator-dependent scores (► **Table 20**, ► **Table 21**, ► **Table 22**). Most of the studies have used different bowel preparation regimens and all except one have used a similar type of capsule. The scores apply different descriptive methods – quantitative and/or qualitative. While quantitative measures apply a numerical score e.g. 1–10, qualitative scores make use of descriptive terms such as adequate and inadequate



► **Fig. 15** MiroView's MapView bar consists of all images from the procedure compressed together, therefore, shows the color of each gastrointestinal tract.



► **Fig. 16** Quantity of bubbles based on GLCM detector strategy. **a** > 10% of image with bubbles. **b** < 10% of image with bubbles.

► **Table 20** Small bowel cleanliness scales: Human operator-dependent scales, quantitative scores.

Reference	Capsule system	Preparation	Assessment parameters	Proportion of video analyzed
Park et al	PillCam	4 L PEG	Proportion of visualized mucosa and degree of obscuration by bubbles, debris, and bile	Consecutive single frames
QI – Brotz et al	PillCam	Clear Liquid diet, overnight fast	QI based on percentage of mucosa visualized, fluid and debris, bubbles, bile/chyme staining, and brightness	Entire video
Spada et al	PillCam	Clear liquid diet, overnight fast or 2 L PEG and simethicone	Proportion of mucosa visualized	Entire video
Oliva et al	PillCam	Clear liquid diet and overnight fast, or 25 or 50 mL/kg of PEG, and/or 20 mL of simethicone	Proportion of mucosa visualized	Consecutive single frames
Van Tuyl et al	PillCam	Clear liquid diet and overnight fast, or 1 L of PEG, or 2 L of PEG	Proportion of mucosa visualized	Segments of video
Caddy et al	–	250 mL sodium picosulphate plus 500 mL PEG with or without erythromycin	Proportion of mucosa visualized	Entire video
Viazis et al	PillCam	Clear Liquid diet and overnight fast, or 2 L PEG	Proportion of unclean mucosa due to intestinal debris	Entire video
Kantianis et al	PillCam	2 and 4 L of PEG	Proportion of mucosa visualized	Consecutive single frames
Chen et al	OMOM	Clear liquid diet and overnight fast, or 250 mL mannitol with or without simethicone	Proportion of mucosa visualized	Consecutive single frames
Rosa et al	PillCam	Clear liquid diet and overnight fast, or 2 L PEG with or without simethicone	Proportion of mucosa visualized	Entire video
Niv et al	PillCam	Clear liquid diet and overnight fast or NaP	Proportion of SBTT with invisible mucosa	Entire video
Alageeli et al	PillCam	Clear liquid diet, overnight fast, 2 L PEG	Proportion of visualized mucosa and degree of obscuration by bubbles, debris, and bile	Consecutive single frames

PEG, polyethylene glycol; NaP, sodium phosphate; SBTT, small bowel transit time.

► **Table 21** Small bowel cleanliness scales: Human operator-dependent scales, qualitative scores.

Reference	Capsule system	Preparation	Assessment parameters	Proportion of video analyzed
OAA – Brotz et al	PillCam	Clear liquid diet, overnight fast	Overall assessment of small-bowel cleansing	Entire video
QE – Brotz et al	PillCam	Clear liquid diet, overnight fast	QE based on percentage of mucosa visualized, fluid and debris, bubbles, bile/chyme staining, and brightness	Entire video
Albert et al	PillCam	Overnight fast or simethicone	Mucosal invisibility due to intraluminal bubbles	Segments of video
Pons Beltrán et al	PillCam	Clear liquid diet, or 90 mL NaP, or 4L of PEG	Amounts of enteric residues	Entire video
Nimomiya et al	PillCam	Clear liquid diet and overnight fast, or citrate magnesium	Bubbles, food residues and intestinal juice colour	Consecutive single frames

NaP, sodium phosphate; PEG, polyethylene glycol.

► **Table 22** Small bowel cleanliness scales: Human operator-dependent scales, quantitative and qualitative scores.

Reference	Capsule system	Preparation	Assessment parameters	Proportion of video analyzed
Esaki et al	PillCam	Simethicone or magnesium citrate	Fluid transparency and proportion of non-visualized mucosa	Entire video
Dai et al	PillCam	4 L PEG or overnight fast	Proportion of visualized mucosa and overall visibility	Segments of video
Lapalus et al	PillCam	Clear liquid diet and overnight fast or NaP	Proportion of visualized mucosa and amounts of enteric liquid and bubbles	Segments of video
Hooks et al	PillCam	Clear liquid diet and overnight fast with or without lubiprostone	Proportion of mucosa visualized and amounts of enteric debris	Entire video and segments of video

PEG, polyethylene glycol; NaP, sodium phosphate.

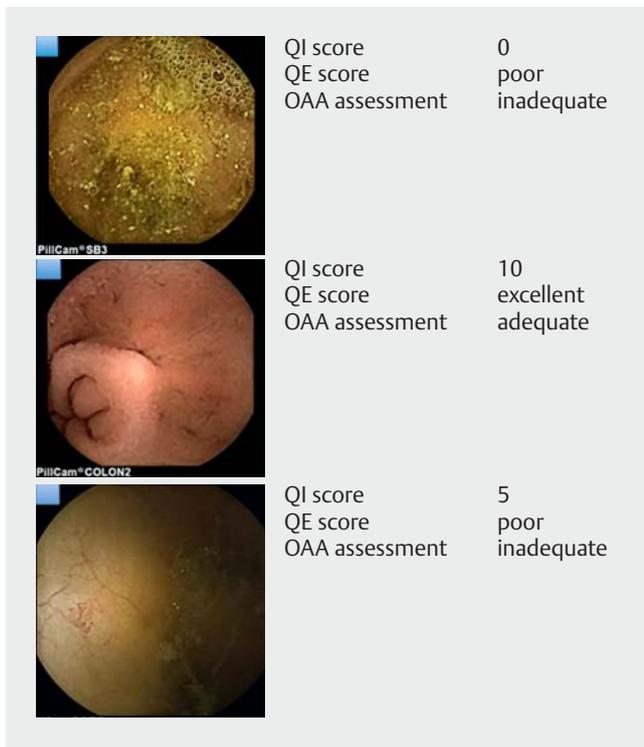
► **Table 23** Brotz Score.

QI					
Points ¹	Percentage of mucosa visualized	Fluid and debris abundance	Bubble abundance	Bile/chyme staining	Brightness reduction
0	<80%	Severe	Severe	Severe	Severe
1	80–89%	Moderate	Moderate	Moderate	Moderate
2	≥90%	Minimal/mild	Minimal/mild	Minimal/mild	Minimal/mild
QE					
Excellent	≥90%	Absent/minimal	Absent/minimal	Absent/minimal	Absent/minimal
Good	≥90%	Mild	Mild	Mild	Mild
Fair	<90%	Moderate	Moderate	Moderate	Moderate
Poor	<80%	Excessive	Excessive	Excessive	Severe
OAA					

Adequate

Inadequate

¹ Total score range 0–10. A high score indicates superior cleansing.



► Fig. 17 Brotz score applied to images from CE.

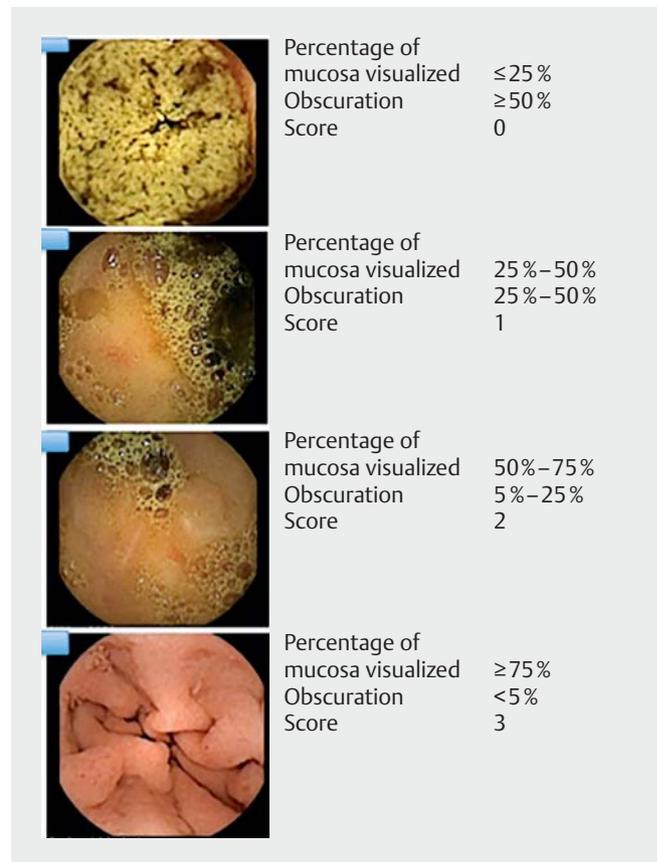
► Table 24 Park score.

Score	0	1	2	3
Percentage of mucosa visualized	≤ 25%	25%–50%	50%–75%	≥ 75%
Obscuration	≥ 50%	25%–50%	5%–25%	< 5%

or poor, fair, good, excellent. Disadvantages for these scores are that they are operator-dependent and all time-consuming. In the absence of a universally accepted score, the two most commonly used scores, which are also mentioned in the ESGE document, on performance measures for SB endoscopy are the validated scores by Park et al. and Brotz et al [117, 118].

The validation study by Brotz et al was a prospective, randomized single-center study. In this study, 40 CE videos (Pill-Cam) were randomized and viewed by five CE readers, who proceeded to score the SB cleanliness based on the three scoring systems previously devised by Brotz et al (► Table 23). A month after the initial scoring, the same 40 CEs were randomly reassigned to the same five readers who reevaluated the SB cleanliness based on the three scores. A clear liquid diet with overnight fast was employed prior to the CE. The three evaluated scales were; a quantitative index (QI 0–10; higher scores corresponding to better cleansing), qualitative evaluation (poor, fair, good, excellent), and overall adequacy assessment (inadequate, adequate). In the evaluation, the QI score used all available frames (► Fig. 17) [22, 117–119].

Park et al developed a cleansing quantitative score based on the proportion of visualized mucosa and the degree of obscura-



► Fig. 18 Park Score applied to images from CE.

tion (► Table 24). In contrast to the former score, the patients were given 4L PEG as bowel preparation. These two visual parameters were scored based on two four-step scales – (a) the proportion of visualized mucosa (0–3) and (b) the degree of obscuration by bubbles, debris, and bile (0–3). These two parameters were evaluated in images from the entire SB selected at 5-minute intervals. The overall score is obtained by summing the scores of all selected images and dividing them by the number of frames examined for each parameter. The final score is the average of the two mean scores. A cut-off value of 2.25 was proposed as adequate SB cleanliness by the authors. The main limitation of this score is that only one frame every 5 minutes is made use of, thus leaving the majority of frames unanalyzed (► Fig. 18) [117].

Today, a validated scale universally accepted for grading SB cleansing is still lacking. In fact, there are numerous grading systems with very different technical characteristics, namely, the parameters and the portion of the CE video that are analyzed, the objectivity of the analysis, the lesser or greater dependency on the operator, and the validation of the score. However, although time-consuming, the operator-dependent scores – Brotz and Park scores should be used during CE interpretation and these are also supported by ESGE (► Table 23, ► Table 24) [22]. The application of these scores will enable the clinician in assessing the reliability of the test, similarly to what is done during colonoscopy [120]. Further research is re-

quired to be able to devise a reliable, reproducible, feasible and preferably automated score.

Conclusions

CE has become the mainstay of non-invasive diagnostic investigation for many diseases affecting the SB. Structured and standardized reporting is critical to improve the description of endoscopic findings and the consistency of image interpretation. The use of standardized scores is helpful in shortening the CE report, minimizing arbitrary or ambiguous descriptions, and summarizing the main findings and conclusions in a clear and clinically relevant manner. With this comprehensive review, we expect to facilitate and guide through using the currently available classification systems for small-bowel CE, as we believe this encloses a valuable potential to improve CE reading, increase the quality of the final report, and ultimately the strength of the recommendations for optimal patients management.

Competing interests

The authors declare that they have no conflict of interest.

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CORRECTION

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In the above-mentioned article the name of Pablo Cortegoso Valdivia was not complete.

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